EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	617	(548/492).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/11/12 16:28
L2	1504	(514/419).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/11/12 16:28
L3	1536	perindopril	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/11/12 16:29
L4	22	l3 and l1	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/11/12 16:29

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1626KAS

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 4	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 6	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 7	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 8	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 9	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 10	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 11	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS 12	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS 13	OCT 19	E-mail format enhanced
NEWS 14	OCT 23	Option to turn off MARPAT highlighting enhancements available
NEWS 15	OCT 23	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 17	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 18	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 19	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 20	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:33:37 ON 12 NOV 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:34:01 ON 12 NOV 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 10 NOV 2006 HIGHEST RN 913001-11-3
DICTIONARY FILE UPDATES: 10 NOV 2006 HIGHEST RN 913001-11-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

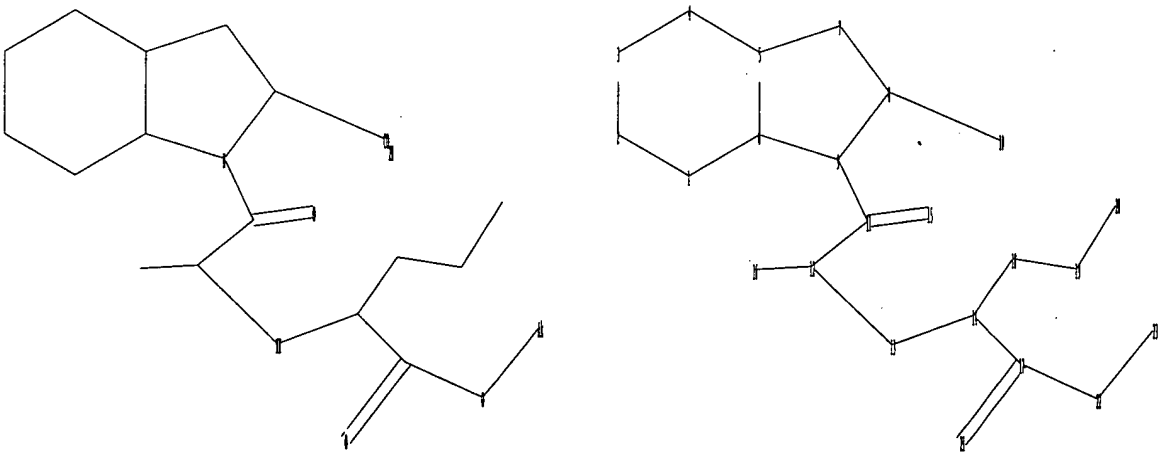
TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10562950.str



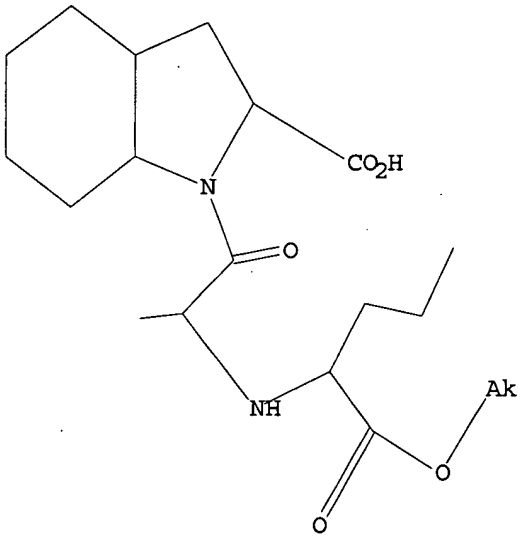
chain nodes :
10 11 12 13 14 15 16 17 18 19 20 21 22 23
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
8-10 9-11 11-12 11-15 12-13 12-16 13-14 14-17 14-18 17-21 17-22 18-19
19-20 22-23

ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 9-11 11-15 12-13 13-14 17-21
17-22 22-23
exact bonds :
8-10 11-12 12-16 14-17 14-18 18-19 19-20

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 16:34:21 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 10377 TO ITERATE

19.3% PROCESSED 2000 ITERATIONS 2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 201436 TO 213644
PROJECTED ANSWERS: 14 TO 400

```
L2            2 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 16:34:28 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   206962 TO ITERATE

100.0% PROCESSED   206962 ITERATIONS                          131 ANSWERS
SEARCH TIME: 00.00.14

L3          131 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                 166.94     167.15

FILE 'CAPLUS' ENTERED AT 16:34:47 ON 12 NOV 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
```

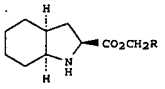


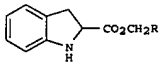
```
FILE COVERS 1907 - 12 Nov 2006  VOL 145 ISS 21
FILE LAST UPDATED: 10 Nov 2006  (20061110/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4          1031 L3

=> s l4 and hydrogenation
          173958 HYDROGENATION
            2270 HYDROGENATIONS
          174192 HYDROGENATION
                 (HYDROGENATION OR HYDROGENATIONS)
L5            41 L4 AND HYDROGENATION

=> d ibib abs hitstr tot
```

L5 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:1038848 CAPLUS
DOCUMENT NUMBER: 145:397363
TITLE: Process for the synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its esters, useful intermediates in the manufacture of perindopril, via resolution of 2,3-dihydroindole-2-carboxylic acid alkyl esters and catalytic hydrogenation of (2S)-2,3-dihydroindole-2-carboxylic acid
INVENTOR(S): Le, Goffic Francois
PATENT ASSIGNEE(S): Laboratoire Substipharm, Fr.
SOURCE: Fr. Demande, 20pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2883874	A1	20061006	FR 2005-3293	20050404
PRIORITY APPLN. INFO.:			FR 2005-3293	20050404

OTHER SOURCE(S): CASREACT 145:397363
GI

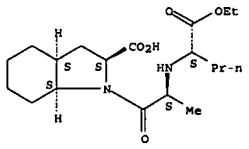

II


III

AB The invention is related to a process for preparation of (-)-(2S,3aS,7aS)-perhydroindole-2-carboxylic acid (I) and its esters II [R = H, alkyl], useful intermediates in the synthesis of perindopril, by (a) enzymic resolution of rac-III [R1 = (un)substituted H, alk(en)yl] by protease-catalyzed hydrolysis to isolate the ester (S)-III and (2R)-2,3-dihydroindole-2-carboxylic acid; (b) saponification or hydrolysis of the ester (S)-III to give (2S)-2,3-dihydroindole-2-carboxylic acid (IV); (c) catalytic hydrogenation of acid IV to give I; (d) isolation of acid I; (e) optionally, esterification of I to give esters of formula II; and (f) isolation of esters II. Advantages include selective preparation of diastereomer acid I in good yield and excellent purity, and simple purification. Thus, acid I was prepared, in > 99% enantiomeric purity, via subtilisin-catalyzed resolution of a mixture of Me 2,3-dihydroindole-2-carboxylate and Et 2,3-dihydroindole-2-carboxylate and hydrogenation of acid IV over Rh/C.

L5 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its esters as useful intermediates in the synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

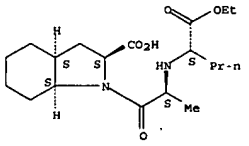
L5 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1311320 CAPLUS
DOCUMENT NUMBER: 144:7101
TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts
INVENTOR(S): Fugier, Claude; Dubuffet, Thierry; Langlois, Pascal
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1367063	A1	20031203	EP 2003-291931	20030731
EP 1367063	B1	20060823		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 337332	E	20060915	AT 2003-291931	20030731
AU 2004261439	A1	20050210	AU 2004-261439	20040729
CA 2533005	AA	20050210	CA 2004-2533005	20040729
WO 2005012333	A2	20050210	WO 2004-FR2035	20040729
WO 2005012333	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1826352	A	20060830	CN 2004-80021209	20040729
BR 2004013169	A	20061003	BR 2004-13169	20040729
US 2006183920	A1	20060817	US 2006-566562	20060131
NO 2006000922	A	20060224	NO 2006-922	20060224
PRIORITY APPLN. INFO.:			EP 2003-291931 A	20030731
			WO 2004-FR2035 W	20040729

OTHER SOURCE(S): MARPAT 144:7101
AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid) involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH2Cl2-EtNPr-i2 at room temperature and MeCN-Et3N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).
IT 82834-16-0P 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril from hexahydroindolecarboxylate and

L5 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
bromopropionyl chloride)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

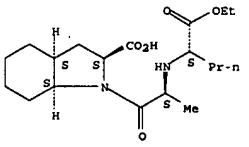


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L5 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

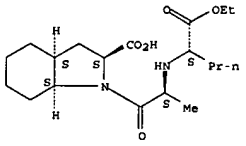
L5 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1311047 CAPLUS
DOCUMENT NUMBER: 144:7100
TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts
INVENTOR(S): Pugier, Claude; Dubuffet, Thierry; Langlois, Pascal
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1367062	A1	20031203	EP 2003-291930	20030731
EP 1367062	B1	20060830		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 338058	E	20060915	AT 2003-291930	20030731
AU 2004261440	A1	20050210	AU 2004-261440	20040729
WO 2005012328	A2	20050210	WO 2004-FR2036	20040729
WO 2005012328	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1826351	A	20060830	CN 2004-80021208	20040729
US 2006189813	A1	20060824	US 2006-566558	20060131
PRIORITY APPLN. INFO.:			EP 2003-291930 A	20030731
			WO 2004-FR2036 W	20040729

OTHER SOURCE(S): CASREACT 144:7100; MARPAT 144:7100
AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH2Cl2-EtNPr-i2 at room temperature and MeCN-Et3N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).
IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

L5 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(Preparation)
(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

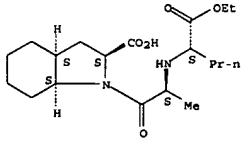


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

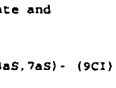
Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L5 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1117891 CAPLUS
DOCUMENT NUMBER: 143:367597
TITLE: Process for the preparation of perindopril
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PATENT ASSIGNEE(S): Neopharma Limited, UK
SOURCE: Brit. UK Pat. Appl., 21 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

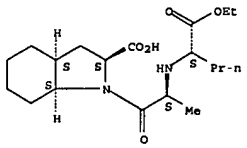
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2413128	A1	20051019	GB 2004-8258	20040413
WO 2005100317	A1	20051027	WO 2005-GB1355	20050407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: GB 2004-8258 A 20040413

OTHER SOURCE(S): MARPAT 143:367597
AB A process for preparing perindopril or a pharmaceutically-acceptable salt comprises coupling a 4-halo-, 4-alkoxy- or 4-nitrobenzyl ester of (2S,3aS,7aS)-2-carboxyoctahydroindole with N-[(S)-1-carbethoxybutyl]-L-alanine (1) in the presence of DCC and HOBT, followed by catalytic hydrolgenolysis. The starting ester was obtained from (S)-indoline-2-carboxylic acid by hydrogenation-esterification and 1 was obtained from norvaline Et ester and pyruvic acid under catalytic hydrogenation conditions. The method was applied to the synthesis perindopril erbumine (20.5 g obtained from 24 g 4-chlorobenzyl ester and 21.26 g 1).
IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril by acylation of octahydroindolecarboxylates with ethoxycarbonylbutylalanine)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

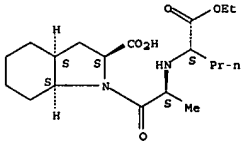


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L5 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:996205 CAPLUS
DOCUMENT NUMBER: 141:395815
TITLE: A process for the preparation of perindopril using tetramethyluronium salts as coupling reagents
INVENTOR(S): Rucman, Rudolf
PATENT ASSIGNEE(S): Lek Pharmaceuticals D.D., Slovenia
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

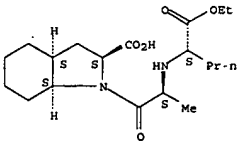
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099236	A1	20041118	WO 2004-SI20	20040507
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21506	C	20041231	SI 2003-118	20030508
EP 1628995	A1	20060301	EP 2004-731809	20040507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: SI 2003-118 A 20030508
WO 2004-SI20 W 20040507

OTHER SOURCE(S): CASREACT 141:395815; MARPAT 141:395815
AB A process for the preparation of the ACE inhibitor perindopril involves activation of N-[1(S)-(ethoxycarbonyl)butyl]-(S)-alanine (1) with a tetramethyluronium salt in the presence of a tertiary organic base, coupling with (2S,3aS,7aS)-octahydroindole-2-carboxylic acid (2) or an ester, and deprotection. Thus, a mixture of 1, 2 benzyl ester, TBTU and diisopropylethylamine in DMF/CH2Cl2 was stirred for 4 h to afford benzyl-perindopril, which was converted to perindopril by phase transfer or classical hydrogenation.
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril using tetramethyluronium salts as coupling reagents)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

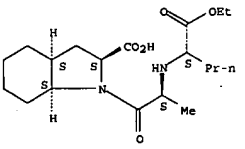


IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril using tetramethyluronium salts as coupling reagents)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L5 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

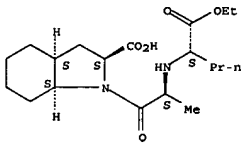
L5 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:740158 CAPLUS
DOCUMENT NUMBER: 141:243833
TITLE: Process for preparation of perindopril and its salts
INVENTOR(S): Datta, Debashish; Singh, Girij Pal; Godbole, Himanshu Madhav; Siyan, Rajinder Singh
PATENT ASSIGNEE(S): Lupin Limited, India
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004075889	A1	20040910	WO 2003-IN42	20030228
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2517205	AA	20040910	CA 2003-2517205	20030228
AU 2003224420	A1	20040917	AU 2003-224420	20030228
EP 1603558	A1	20051214	EP 2003-720846	20030228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006519168	T2	20060824	JP 2004-568714	20030228
PRIORITY APPLN. INFO.:			WO 2003-IN42 W	20030228

OTHER SOURCE(S): CASREACT 141:243833; MARPAT 141:243833
AB A process for the preparation of perindopril and its salts involves reaction of N-[1(S)-(ethoxycarbonyl)butyl]-L-alanyl chloride (I) or bromide with (2S)-indolinecarboxylic acid benzyl ester or its hexahydro derivative, followed by catalytic hydrogenation. Thus, perindopril benzyl ester was prepared by adding a slurry of 1.88 g I (preparation given) to a solution of 1.6 g (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester and triethylamine in CH2Cl2 at -10 to 15° over 25-30 min. Hydrogenation of the benzyl ester over 10% Pd-C afforded 1.3 g perindopril.
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril and its salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:427629 CAPLUS
DOCUMENT NUMBER: 140:407114
TITLE: Method for synthesis of perindopril and its pharmaceutically-acceptable salts
INVENTOR(S): Dubuffet, Thierry; Langlois, Pascal
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

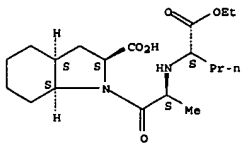
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1422236	A1	20040526	EP 2003-292865	20031119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
WO 2005054277	A1	20050616	WO 2004-FR2937	20041118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-292865 A 20031119

OTHER SOURCE(S): MARPAT 140:407114
AB Perindopril was prepared by cyclization of (2S)-3-(2-bromophenyl)-2-{[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]propanoyl]amino}propanoic acid (I) or its esters in the presence of a Pd-based catalyst and a base (e.g., Pd2(dba)3, P(o-tolyl)3, and Cs2CO3], followed by catalytic hydrogenation. Intermediate I was prepared by coupling of N-[(S)-1-carbethoxybutyl]-L-alanine N-carboxyanhydride with (S)-2-bromophenylalanine.
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

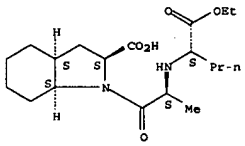


IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



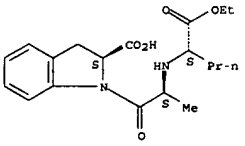
CM 2

CRN 75-64-9
CMF C4 H11 N

L5 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

IT 685141-30-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 685141-30-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3-dihydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:405664 CAPLUS
DOCUMENT NUMBER: 140:375492
TITLE: Method for synthesis of (2S,3aS,7aS)-1-[(S)-alanyl]octahydro-1H-indole-2-carboxylic acid derivatives and use in the synthesis of perindopril
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

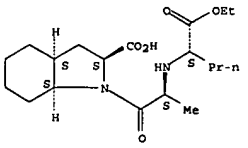
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1420030	A2	20040519	EP 2003-293085	20031210
EP 1420030	A3	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004312186	A1	20050721	AU 2004-312186	20041209
CA 2548406	AA	20050721	CA 2004-2548406	20041209
WO 2005066199	A1	20050721	WO 2004-FR3167	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NO 2006003027	A	20060628	NO 2006-3027	20060628

PRIORITY APPLN. INFO.: EP 2003-293085 A 20031210
WO 2004-FR3167 W 20041209

OTHER SOURCE(S): CASREACT 140:375492; MARPAT 140:375492
AB A method for the synthesis of the title perindopril intermediate involves coupling of (2S)-indoline-2-carboxylic acid benzyl ester or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester or their salts with N-protected L-alanine in the presence of a coupling agent [e.g., O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate], followed by hydrogenation over Pd.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of alanyloctahydroindolecarboxylic acid derivs. in synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



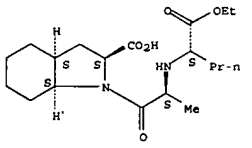
L5 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:405663 CAPLUS
DOCUMENT NUMBER: 140:375491
TITLE: Method for the synthesis of perindopril and its pharmaceutically-acceptable salts
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1420029	A2	20040519	EP 2003-293084	20031210
EP 1420029	A3	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004312185	A1	20050721	AU 2004-312185	20041209
CA 2548405	AA	20050721	CA 2004-2548405	20041209
WO 2005066198	A1	20050721	WO 2004-FR3166	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NO 2006003012	A	20060628	NO 2006-3012	20060628
PRIORITY APPLN. INFO.:			EP 2003-293084 A	20031210
			WO 2004-FR3166 W	20041209

OTHER SOURCE(S): CASREACT 140:375491
AB A method for the synthesis of perindopril involves coupling of (2S)-indoline-2-carboxylic acid benzyl ester or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester with N-[(S)-1-carbethoxybutyl]-L-alanine in the presence of a coupling agent [e.g., O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate], followed by hydrogenation over Pd. Perindopril was converted into its tert-butylamine salt.
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

L5 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).

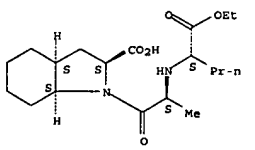


IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

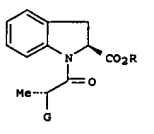
CRN 75-64-9
CMF C4 H11 N

L5 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:405662 CAPLUS
DOCUMENT NUMBER: 140:375490
TITLE: Method for the synthesis of perindopril and its pharmaceutically-acceptable salts
INVENTOR(S): Dubuffet, Thierry; Langlois, Pascal
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1420028	A2	20040519	EP 2003-292864	20031119
EP 1420028	A3	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004295132	A1	20050616	AU 2004-295132	20041118
CA 2546506	AA	20050616	CA 2004-2546506	20041118
WO 2005054276	A1	20050616	WO 2004-FR2936	20041118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NO 2006002599	A	20060606	NO 2006-2599	20060606
PRIORITY APPLN. INFO.:			EP 2003-292864 A	20031119
			WO 2004-FR2936 W	20041118

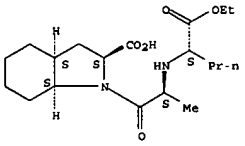
OTHER SOURCE(S): CASREACT 140:375490; MARPAT 140:375490
GI



AB A method for the synthesis of perindopril involves reaction of indolinecarboxylate derivs. I (R = H or a protective group, G = Cl, Br, OH, TsO, MeSO3 or CF3SO3) with (S)-PrCH(NH2)CO2Et (II), followed by catalytic hydrogenation. II was prepared by reaction of

L5 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(S)-2-BrC6H4CH2CH(NH2)CO2R with (R)-MeCH(G)COCl and intramol. coupling, e.g., in the presence of Pd2(dba)3, P(o-tolyl)3, and Cs2CO3. Perindopril was converted into its tert-butylamine salt.
IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

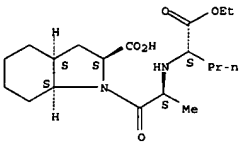


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

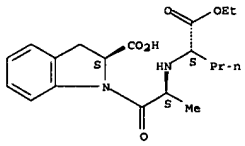


CM 2

L5 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CRN 75-64-9
CMF C4 H11 N

IT 685141-30-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 685141-30-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3-dihydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 11 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:266899 CAPLUS
DOCUMENT NUMBER: 140:253919
TITLE: Process for the synthesis of N-[(S)-1-(ethoxycarbonyl)butyl]-(S)-alanine for use in the synthesis of perindopril
INVENTOR(S): Breard, Fabienne; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

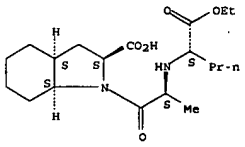
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1403278	A1	20040331	EP 2003-292404	20030930
EP 1403278	B1	20050608		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 297407	E	20050615	AT 2003-292404	20030930
PT 1403278	T	20050930	PT 2003-292404	20030930
ES 2240926	T3	20051016	ES 2003-3292404	20030930
WO 2005033127	A1	20050414	WO 2004-FR2463	20040929
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-292404 A 20030930

OTHER SOURCE(S): MARPAT 140:253919
AB Perindopril intermediate (S)-EtO2CCHPr-L-Ala-OH was prepared by condensation of L-alanine alkyl or benzyl ester with Et glyoxylate or Et chloro(cyclohexyloxy)acetate, followed by allylation with allylzinc bromide, and catalytic hydrogenation.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of [(ethoxycarbonyl)butyl]alanine for use in preparation of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 11 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

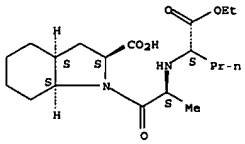
L5 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:266898 CAPLUS
DOCUMENT NUMBER: 140:253918
TITLE: Method for synthesis of (2S,3aS,7aS)-1-[(S)-alanyl]octahydro-1H-indole-2-carboxylic acid derivatives for use in the synthesis of perindopril
INVENTOR(S): Dubuffet, Thiery; Langlois, Pascal
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.; Servier Lab
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1403277	A1	20040331	EP 2003-290486	20030228
EP 1403277	B1	20051005		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 305939	E	20051015	AT 2003-290486	20030228
PT 1403277	T	20051130	PT 2003-290486	20030228
ES 2249691	T3	20060401	ES 2003-290486	20030228
AU 2004218202	A1	20040916	AU 2004-218202	20040227
WO 2004078708	A2	20040916	WO 2004-FR445	20040227
WO 2004078708	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1753907	A	20060329	CN 2004-80005406	20040227
JP 2006519176	T2	20060824	JP 2006-500162	20040227
US 2006149082	A1	20060706	US 2005-547132	20050824
PRIORITY APPLN. INFO.:			EP 2003-290486 A	20030228
			WO 2004-FR445 A	20040227

OTHER SOURCE(S): CASREACT 140:253918; MARPAT 140:253918
AB A method for the synthesis of title perindopril intermediate involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indolecarboxylic acid (I) or an alkyl or benzyl ester with N-protected alanine, followed by catalytic hydrogenation. I benzyl ester was prepared by reaction of 1-(1-cyclohexen-1-yl)pyrrolidine with (R)-ICH2CH(NBoc)CO2CH2Ph (Boc = tert-butoxycarbonyl), followed by deprotection and cyclization.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of alanyloctahydroindolecarboxylic acid derivs. for synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)

L5 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

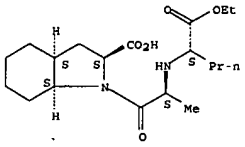
L5 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:266897 CAPLUS
DOCUMENT NUMBER: 140:253917
TITLE: Process for the synthesis of perindopril and its pharmaceutically-acceptable salts
INVENTOR(S): Dubuffet, Thierry; Langlois, Pascal
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1403275	A1	20040331	EP 2003-290485	20030228
EP 1403275	B1	20051019		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 307139	E	20051115	AT 2003-290485	20030228
ES 2250846	T3	20060416	ES 2003-290485	20030228
AU 2004217599	A1	20040916	AU 2004-217599	20040227
WO 2004078107	A2	20040916	WO 2004-FR446	20040227
WO 2004078107	A3	20041021		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1753906	A	20060329	CN 2004-80005405	20040227
JP 2006519177	T2	20060824	JP 2006-500163	20040227
US 2006149081	A1	20060706	US 2005-547131	20050824
PRIORITY APPLN. INFO.:			EP 2003-290485 A	20030228
			WO 2004-FR446 A	20040227

OTHER SOURCE(S): MARPAT 140:253917
AB A method for the synthesis of perindopril involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indolecarboxylic acid (I) or an ester with N-[(S)-1-carbethoxybutyl]-L-alanine, followed by catalytic hydrogenation. I benzyl ester tosylate was prepared by reaction of 1-(1-cyclohexen-1-yl)pyrrolidine with (R)-ICH2CH(NBoc)CO2CH2Ph (Boc = tert-butoxycarbonyl), followed by deprotection and cyclization. Perindopril was converted into its tert-butylamine salt.
IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril and pharmaceutically-acceptable salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

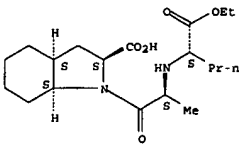


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

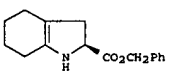
CRN 75-64-9
CMF C4 H11 N

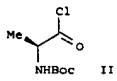
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 14 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:36709 CAPLUS
DOCUMENT NUMBER: 140:59939
TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.; Servier Lab
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1380591	A1	20040114	EP 2003-292132	20030829
EP 1380591	B1	20051116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 310012	E	20051215	AT 2003-292132	20030829
ES 2252633	T3	20060516	ES 2003-3292132	20030829
AU 2004270428	A1	20050317	AU 2004-270428	20040827
WO 2005023842	A1	20050317	WO 2004-FR2197	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1835966	A	20060920	CN 2004-80023535	20040827
PRIORITY APPLN. INFO.:			EP 2003-292132 A	20030829
			WO 2004-FR2197 W	20040827

OTHER SOURCE(S): CASREACT 140:59939; MARPAT 140:59939
GI


I


II

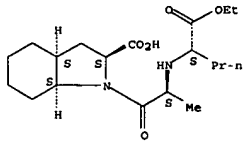
AB A method for the synthesis of perindopril and its tert-Bu amine salt is described. The steps are: coupling of hexahydroindolecarboxylate I with propionyl chloride II in CH2Cl2, followed by Boc deprotection with TFA and

L5 ANSWER 14 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CMF C4 H11 N

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 14 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
reaction with Et 2-oxopentanoate and hydrogenation over Pd/C. Addn. of tert-butylamine to perindopril provides the salt.
IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of perindopril and tert-butylamine salt)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

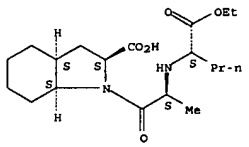


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

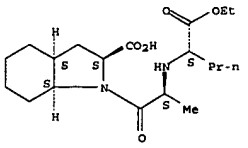
L5 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:36708 CAPLUS
DOCUMENT NUMBER: 140:59938
TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1380590	A1	20040114	EP 2003-292131	20030829
EP 1380590	B1	20060906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 338766	E	20060915	AT 2003-292131	20030829
AU 2004270427	A1	20050317	AU 2004-270427	20040827
WO 2005023841	A1	20050317	WO 2004-FR2196	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1839147	A	20060927	CN 2004-80024192	20040827
PRIORITY APPLN. INFO.:			EP 2003-292131 A	20030829
			WO 2004-FR2196 W	20040827

OTHER SOURCE(S): CASREACT 140:59938; MARPAT 140:59938
AB A method for the synthesis of perindopril and its pharmaceutically-acceptable salts involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indolecarboxylic acid or its benzyl ester with R2-L-Ala-X (R2 is a protective group, X is halo), followed by deprotection, reaction with (R)-PrCH(G)CO2Et (G is Cl, Br, I, or tosyloxy), and catalytic hydrogenation. Addition of tert-butylamine to perindopril provides the salt.
IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of perindopril and tert-butylamine salt)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

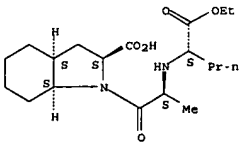


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd.
with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

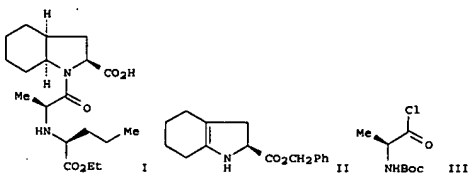
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L5 ANSWER 16 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:985781 CAPLUS
DOCUMENT NUMBER: 140:28049
TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts [2003/26]
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.; Servier Lab
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1371659	A1	20031217	EP 2003-292133	20030829
EP 1371659	B1	20051012		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 306496	E	20051015	AT 2003-292133	20030829
ES 2250853	T3	20060416	ES 2003-3292133	20030829
AU 2004270429	A1	20050317	AU 2004-270429	20040827
WO 2005023843	A1	20050317	WO 2004-FR2198	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1835965	A	20060920	CN 2004-80023532	20040827
PRIORITY APPLN. INFO.:			EP 2003-292133	A 20030829
			WO 2004-FR2198	W 20040827

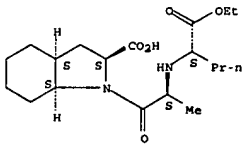
OTHER SOURCE(S): CASREACT 140:28049; MARPAT 140:28049
GI



L5 ANSWER 16 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

AB A method for the synthesis of perindopril (I) and its tert-Bu amine salt is described. The steps are: coupling of (hexahydro)indolecarboxylate II with propionyl chloride III in CH2Cl2, followed by Boc deprotection with TFA, reaction with Et 2-oxopentanoate under reductive conditions, and removal of benzyl ester by hydrogenation to give I. Addition of tert-Bu amine to I provides the salt.
IT 82834-16-0P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril and its tert-Bu amine salt)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

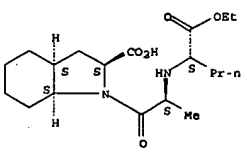


IT 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril and its tert-Bu amine salt)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd.
with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



L5 ANSWER 16 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 75-64-9
CMF C4 H11 N

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L5 ANSWER 17 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:947713 CAPLUS
DOCUMENT NUMBER: 139:381760
TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1367061	A1	20031203	EP 2003-291601	20030630
EP 1367061	B1	20060104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 315043	E	20060215	AT 2003-291601	20030630
ES 2256689	T3	20060716	ES 2003-3291601	20030630
AU 2004253721	A1	20050113	AU 2004-253721	20040628
WO 2005003153	A1	20050113	WO 2004-FR1637	20040628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1802384	A	20060712	CN 2004-80016014	20040628
US 2006178421	A1	20060810	US 2005-562490	20051222
PRIORITY APPLN. INFO.:			EP 2003-291601 A	20030630
			WO 2004-FR1637 W	20040628

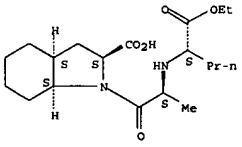
OTHER SOURCE(S): CASREACT 139:381760; MARPAT 139:381760

AB A method for the synthesis of perindopril and its pharmaceutically-acceptable salts (e.g., the tert-butylamine) involves cyclocondensation reaction of N-[(S)-1-carbethoxybutyl]-(S)-alanine with sulfinyl chlorides R1SOCl (R1 = imidazolyl, benimidazolyl, or tetrazolyl) to give Et (2S)-2-[(4S)-4-methyl-2,5-dioxo-1,2,3-oxathiazolidin-3-yl]pentanoate, which is amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid and hydrogenated over 10% Pt/C to give perindopril.

IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril via cyclocondensation of carbethoxybutylalanine with imidazolesulfinyl chloride)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

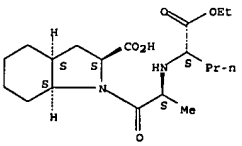


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

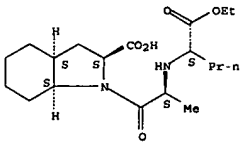
L5 ANSWER 18 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:910218 CAPLUS
DOCUMENT NUMBER: 139:365227
TITLE: New process for the synthesis of N-[(S)-1-carboxybutyl]-(S)-alanine esters and their use in the synthesis of perindopril
INVENTOR(S): Breard, Fabienne; Fugier, Claude
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1362845	A2	20031119	EP 2003-292145	20030901
EP 1362845	A3	20040331		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004270432	A1	20050317	AU 2004-270432	20040831
CA 2536926	AA	20050317	CA 2004-2536926	20040831
WO 2005023755	A1	20050317	WO 2004-FR2213	20040831
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1835911	A	20060920	CN 2004-80023534	20040831
US 2006252958	A1	20061109	US 2006-569472	20060222
NO 2006001152	A	20060310	NO 2006-1152	20060310
PRIORITY APPLN. INFO.:			EP 2003-292145 A	20030901
			WO 2004-FR2213 W	20040831

OTHER SOURCE(S): CASREACT 139:365227; MARPAT 139:365227
AB Title alanine deriva. (S)-RO2CCHPr-L-Ala-OH (R = C1-C6 alkyl) were prepared from N-protected (S)-5-methyl-2-morpholinone by propylation or allylation/ hydrogenation, ring opening by LiOH, esterification, oxidation of the hydroxy group, and deprotection. In an example, N-[(S)-1-carbethoxybutyl]-(S)-alanine hydrochloride was prepared via allylation of Boc-protected (S)-5-methyl-2-morpholinone and treatment of tert-Bu (3S,5S)-5-methyl-3-propyl-2-oxo-4-morpholinecarboxylate with LiOH in aqueous MeCN and then EtI to afford intermediate Et (2S)-2-[(tert-butoxycarbonyl)[(1S)-2-hydroxy-1-methylethyl]amino]pentanoate.

L5 ANSWER 18 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(process for synthesis of N-[(S)-carboxybutyl]-L-alanine esters for use in synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



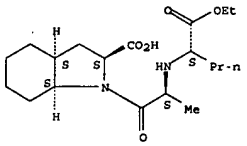
L5 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:909172 CAPLUS
DOCUMENT NUMBER: 139:396166
TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1362864	A1	20031119	EP 2003-291600	20030630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004255899	A1	20050120	AU 2004-255899	20040628
WO 2005005461	A2	20050120	WO 2004-FR1638	20040628
WO 2005005461	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1805972	A	20060719	CN 2004-80016324	20040628
US 2006148884	A1	20060706	US 2005-562950	20051223
PRIORITY APPLN. INFO.:			EP 2003-291600 A	20030630
			WO 2004-FR1638 W	20040628

OTHER SOURCE(S): CASREACT 139:396166; MARPAT 139:396166
AB Perindopril and its pharmaceutically acceptable salts (e.g., tert-butylamine salt) are prepared by the cyclocondensation reaction of N-[(S)-carboethoxy-1-butyl]-(S)-alanine with a carbonyl compound X1COX2 (X1, X2 = leaving group; e.g., 1,1'-carbonyldiimidazole) to give Et (2S)-2-[(4S)-4-Methyl-2,5-dioxo-1,3-oxazolidin-3-yl]pentanoate which is amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid in the presence of an acid (e.g., hydrochloric acid) to give (2S)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid which is hydrogenated with a 10% Pt/C catalyst to give perindopril which is then salified with tert-butylamine to give perindopril tert-butylammonium salt.
IT 82834-16-0P, Perindopril
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for synthesis of perindopril and its pharmaceutically acceptable salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)

L5 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

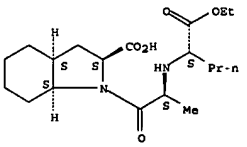


IT 107133-36-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(method for synthesis of perindopril and its pharmaceutically acceptable salts)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L5 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 20 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:832153 CAPLUS
DOCUMENT NUMBER: 139:308016
TITLE: Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril
INVENTOR(S): Dubuffet, Thierry; Langlois, Pascal
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

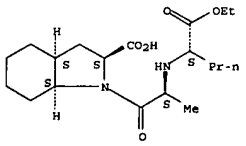
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1354876	A1	20031022	EP 2003-291420	20030613
EP 1354876	B1	20050427		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 294161	E	20050515	AT 2003-291420	20030613
PT 1354876	T	20050630	PT 2003-291420	20030613
ES 2240921	T3	20051016	ES 2003-3291420	20030613
WO 2005003091	A1	20050113	WO 2004-FR1427	20040609
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-291420 A 20030613

OTHER SOURCE(S): MARPAT 139:308016
AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its alkyl esters, intermediates used in the synthesis of perindopril, were prepared by condensation of 2-(hydroxymethyl)cyclohexanone with glycine benzyl or alkyl ester to give (2RS,3aRS)-3,3a,4,5,6,7-hexahydro-2H-indole-2-carboxylic acid esters, which underwent catalytic hydrogenation of the double bond and resolution using a chiral amine. In an example, (2S,3aS,7aS)-perhydroindole-2-carboxylic acid was prepared with chemical purity 98% and enantiomeric purity 99%.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as perindolpril intermediates)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)

L5 ANSWER 20 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



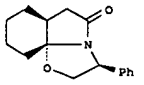
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 21 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:832152 CAPLUS
DOCUMENT NUMBER: 139:308015
TITLE: Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1354875	A1	20031022	EP 2003-291157	20030519
EP 1354875	B1	20041124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 283258	E	20041215	AT 2003-291157	20030519
PT 1354875	T	20050331	PT 2003-291157	20030519
ES 2233914	T3	20050616	ES 2003-3291157	20030519
WO 2004103969	A1	20041202	WO 2004-FR1225	20040519
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-291157 A 20030519

OTHER SOURCE(S): CASREACT 139:308015; MARPAT 139:308015
GI

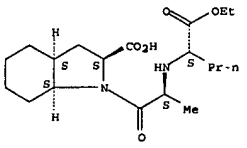


I

AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its alkyl or benzyl esters, intermediates used in the synthesis of perindopril, were prepared by condensation of (2-oxocyclohexyl)acetic acid with (S)-phenylglycinol to

L5 ANSWER 21 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
give lactam I, reductive ring opening of the oxazole ring, cleavage of the
2-hydroxy-1-phenylethyl group, reaction with triflic anhydride, cyanation,
hydrolysis of the cyano group, and hydrogenation of the double bond. In an example, (2S,3aS,7aS)-perhydroindole-2-carboxylic acid was obtained as the tosylate in enantiomeric purity 99%.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as perindopril intermediates)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

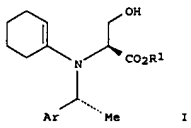


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:832151 CAPLUS
DOCUMENT NUMBER: 139:308014
TITLE: Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril
INVENTOR(S): Dubuffet, Thierry; Langlois, Pascal
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1354874	A1	20031022	EP 2003-290931	20030415
EP 1354874	B1	20041124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 283257	E	20041215	AT 2003-290931	20030415
PT 1354874	T	20050331	PT 2003-290931	20030415
ES 2233913	T3	20050616	ES 2003-3290931	20030415
WO 2004092133	A1	20041028	WO 2004-FR858	20040407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			EP 2003-290931	A 20030415

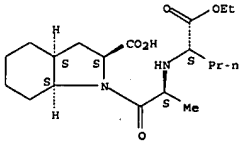
OTHER SOURCE(S): CASREACT 139:308014; MARPAT 139:308014
GI



L5 ANSWER 22 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its alkyl or benzyl esters, intermediates used in the synthesis of perindopril, were prepared by
condensation of L-serine alkyl or benzyl ester with acetophenone derivs. ArCOMe (Ar = alkylphenyl or naphthyl), reduction of the imine formed, reaction
with cyclohexanone to give I, halodehydroxylation, radical cyclization, and deprotection. In an example, (2S,3aS,7aS)-perhydroindole-2-carboxylic
acid was obtained with chemical purity 98% and enantiomeric purity 99%.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as perindopril intermediates)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



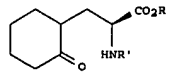
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:675553 CAPLUS
DOCUMENT NUMBER: 139:197771
TITLE: Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril
INVENTOR(S): Dubuffet, Thierra; Langlois, Pascal
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.; Servier Lab
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

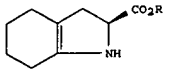
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1338591	A1	20030827	EP 2003-290487	20030228
EP 1338591	B1	20051026		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 307801	E	20051115	AT 2003-290487	20030228
ES 2250847	T3	20060416	ES 2003-290487	20030228
AU 2004218200	A1	20040916	AU 2004-218200	20040227
WO 2004078707	A2	20040916	WO 2004-FR444	20040227
WO 2004078707	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1753869	A	20060329	CN 2004-80005407	20040227
JP 2006519175	T2	20060824	JP 2006-500161	20040227
US 2006167273	A1	20060727	US 2005-546967	20050824
PRIORITY APPLN. INFO.:			EP 2003-290487	A 20030228
			WO 2004-FR444	A 20040227

OTHER SOURCE(S): CASREACT 139:197771; MARPAT 139:197771
GI

L5 ANSWER 23 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



I



II

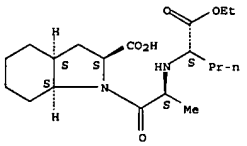
AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its benzyl or alkyl esters were prepared by reaction of 1-(1-cyclohexen-1-yl)pyrrolidine with (R)-ICH2CH(NR')CO2R (R is H, benzyl, or alkyl; R' is an amine-protecting group) to afford cyclohexanone derivs. I. Cyclization of I, e.g., using p-toluenesulfonic acid, gave compds. II, which underwent catalytic hydrogenation to afford compds. of the invention. The title acid was obtained in 87% yield and 99% enantiomeric purity by this method.

IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(method for synthesis of perhydroindolecarboxylic acid and esters as perindopril intermediates)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

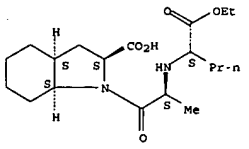
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L5 ANSWER 24 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



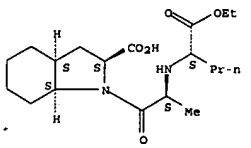
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT.

L5 ANSWER 24 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:488613 CAPLUS
DOCUMENT NUMBER: 139:22503
TITLE: Method for the synthesis of perindopril and its pharmaceutically-acceptable salts
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1321471	A1	20030625	EP 2003-290605	20030312
EP 1321471	B1	20050504		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 294814	E	20050515	AT 2003-290605	20030312
PT 1321471	T	20050729	PT 2003-290605	20030312
ES 2240919	T3	20051016	ES 2003-3290605	20030312
WO 2004083238	A1	20040930	WO 2004-FR594	20040312
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-290605 A 20030312

OTHER SOURCE(S): CASREACT 139:22503; MARPAT 139:22503

AB Perindopril and its pharmaceutically-acceptable salts were prepared from 2,7-oxepanedione by a multistep procedure, i.e., reaction with (R)-XCH2CH(NHBoc)CO2CH2Ph (X is Br or iodo; Boc is tert-butoxycarbonyl), cyclization of deprotected 2-amino-4-oxononanedioic acid derivative, Ti-catalyzed coupling to form the indole ring system, reaction with N-[(S)-1-carbethoxybutyl]-(S)-alanine, and catalytic hydrogenation . In an example, perindopril was obtained with enantiomeric purity 99%.

IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(method for synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 25 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN

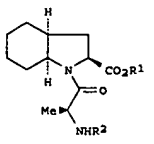
ACCESSION NUMBER: 2003:470308 CAPLUS
DOCUMENT NUMBER: 139:22502
TITLE: Method for the synthesis of (2S,3aS,7aS)-1-[(S)-alanyl]octahydro-1H-indole-2-carboxylic acid derivatives for use in the synthesis of perindopril
INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1319668	A1	20030618	EP 2003-290606	20030312
EP 1319668	B1	20041027		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 280775	E	20041115	AT 2003-290606	20030312
PT 1319668	T	20050228	PT 2003-290606	20030312
ES 2231759	T3	20050516	ES 2003-3290606	20030312
WO 2004082357	A2	20040930	WO 2004-FR593	20040312
WO 2004082357	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-290606 A 20030312

OTHER SOURCE(S): CASREACT 139:22502; MARPAT 139:22502

GI

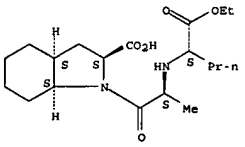


I

AB Alanyloctahydroindolecarboxylic acid derivs. I (R1 is H, alkyl, or benzyl;

L5 ANSWER 25 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
R2 is a protecting group) were prepd. from 2,7-oxepanedione by a multistep
procedure, i.e., reaction with (R)-XCH2CH(NHR3)CO2R4 (X is Br or iodo; R3 is a protecting group; R4 is benzyl or alkyl), cyclization of deprotected 2-amino-4-oxononanedioic acid deriv., Ti-catalyzed coupling to form the indole ring system, reaction with an alanine derivs., and catalytic hydrogenation. In an example, I (R1 = H, R2 = tert-butoxycarbonyl) was obtained with enantiomeric purity 99%.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of alanyloctahydroindolecarboxylic acid derivs. for use in synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

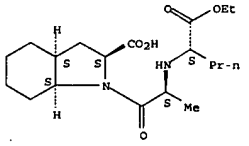
L5 ANSWER 26 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:597957 CAPLUS
DOCUMENT NUMBER: 135:167034
TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts
INVENTOR(S): Langlois, Pascal; Turbe, Hugues
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058868	A1	20010816	WO 2001-FR1026	20010405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2807431	A1	20011012	FR 2000-4379	20000406
FR 2807431	B1	20020719		
CA 2405486	AA	20010816	CA 2001-2405486	20010405
AU 2001048470	A5	20010820	AU 2001-48470	20010405
EP 1268424	A1	20030102	EP 2001-921486	20010405
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001009836	A	20030624	BR 2001-9836	20010405
JP 2003531825	T2	20031028	JP 2001-558419	20010405
NZ 521454	A	20040326	NZ 2001-521454	20010405
EE 200200575	A	20040415	EE 2002-575	20010405
ZA 2002007419	A	20030916	ZA 2002-7419	20020916
US 2003069431	A1	20030410	US 2002-239129	20020919
US 6835843	B2	20041228		
NO 2002004808	A	20021004	NO 2002-4808	20021004
BG 107249	A	20030731	BG 2002-107249	20021104
PRIORITY APPLN. INFO.:			FR 2000-4379 A	20000406
			WO 2001-FR1026 W	20010405

OTHER SOURCE(S): CASREACT 135:167034
AB Perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] was prepared by coupling (2S,3aS,7aS)octahydroindole-2-carboxylic acid tosylate with N-[(S)-1-carbethoxybutyl]-(S)-alanine, followed by catalytic hydrogenation to remove the benzyl group. In an example, the coupling reaction was carried out in Et acetate in the presence of Et3N, 1-hydroxybenzotriazole and dicyclohexylcarbodiimide at 30° for 3h to give 92% perindopril benzyl ester.

L5 ANSWER 26 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

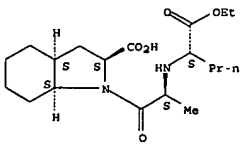


IT 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(method for synthesis of perindopril)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

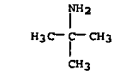
Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L5 ANSWER 26 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:581830 CAPLUS
DOCUMENT NUMBER: 135:137713
TITLE: Synthesis of N-[(S)-1-carboxybutyl]-(S)-alanine esters
for synthesis of perindopril
INVENTOR(S): Souvie, Jean-Claude; Renaud, Alain
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

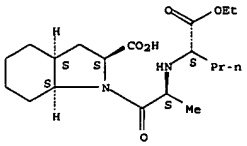
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001056972	A1	20010809	WO 2001-FR1088	20010410
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2807430	A1	20011012	FR 2000-4610	20000411
FR 2807430	B1	20020517		
CA 2405466	AA	20010809	CA 2001-2405466	20010410
CA 2405466	C	20050215		
EP 1272454	A1	20030108	EP 2001-923776	20010410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003521530	T2	20030715	JP 2001-556822	20010410
BR 2001009963	A	20030805	BR 2001-9963	20010410
EE 200200586	A	20040415	EE 2002-586	20010410
NZ 521846	A	20040730	NZ 2001-521846	20010410
ZA 2002007689	A	20030925	ZA 2002-7689	20020925
NO 2002004811	A	20021004	NO 2002-4811	20021004
US 2003109743	A1	20030612	US 2002-257239	20021009
US 6774259	B2	20040810		
BG 107250	A	20030630	BG 2002-107250	20021104
HK 1053300	A1	20050401	HK 2003-105540	20030801

PRIORITY APPLN. INFO.: FR 2000-4610 A 20000411
WO 2001-FR1088 W 20010410

OTHER SOURCE(S): CASREACT 135:137713; MARPAT 135:137713
AB Title alanine derivs. (S)-RO2CCHPr-L-Ala-OH (R = C1-C6 alkyl) were prepared
by condensation of L-alanine with PrCOCO2R under hydrogen pressure and 5% Pd/C as catalyst. In an example, hydrogenation of a mixture of 25 kg L-alanine, 1.1 kg soda and 36 kg Et 2-oxopentanoate in H2O over 5% Pd/C
at room temperature and 1 bar pressure afforded N-[(S)-1-carbethoxybutyl]-(S)-

L5 ANSWER 27 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
alanine.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of [carboxybutyl]alanine esters for synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 28 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:581647 CAPLUS
DOCUMENT NUMBER: 135:137711
TITLE: Synthesis of N-[(S)-1-carboxybutyl]-(S)-alanine esters
for synthesis of perindopril
INVENTOR(S): Souvie, Jean-Claude
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: PCT Int. Appl., 8 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

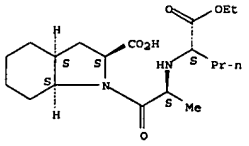
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001056353	A2	20010809	WO 2001-FR959	20010330
WO 2001056353	A3	20020418		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2807037	A1	20011005	FR 2000-4112	20000331
FR 2807037	B1	20020510		
CA 2404700	AA	20010809	CA 2001-2404700	20010330
AU 2001048433	A5	20010814	AU 2001-48433	20010330
EP 1268398	A2	20030102	EP 2001-921440	20010330
EP 1268398	B1	20050608		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003534241	T2	20031118	JP 2001-556065	20010330
BR 2001009609	A	20040113	BR 2001-9609	20010330
NZ 521324	A	20040326	NZ 2001-521324	20010330
EE 200200553	A	20040415	EE 2002-553	20010330
AU 2001248433	B2	20041028	AU 2001-248433	20010330
AT 297377	E	20050615	AT 2001-921440	20010330
PT 1268398	T	20050930	PT 2001-921440	20010330
ES 2242743	T3	20051116	ES 2001-1921440	20010330
ZA 2002007150	A	20030905	ZA 2002-7150	20020905
US 2003045744	A1	20030306	US 2002-221973	20020916
US 6818788	B2	20041116		
NO 2002004616	A	20020926	NO 2002-4616	20020926
BG 107234	A	20030731	BG 2002-107234	20021030
HK 1053301	A1	20050318	HK 2003-105541	20030801

PRIORITY APPLN. INFO.: FR 2000-4112 A 20000331
WO 2001-FR959 W 20010330

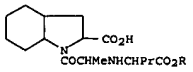
OTHER SOURCE(S): CASREACT 135:137711; MARPAT 135:137711
AB Title alanine derivs. (S)-RO2CCHPr-L-Ala-OH (R = C1-C6 alkyl) were prepared
by condensation of sodium pyruvate with (S)-RO2CCHPrNH2.HCl under hydrogen
pressure and 5% Pd/C as catalyst. In an example, hydrogenation

L5 ANSWER 28 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
of a mixt. of 3 kg (S)-Et norvalinate hydrochloride and 2 kg sodium pyruvate in NaOH aq. soln. over 5% Pd/C at 35° and 1.2 bar pressure afforded 62% N-[(S)-1-carbethoxybutyl]-(S)-alanine.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of (carboxybutyl)alanine esters for synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:73362 CAPLUS
DOCUMENT NUMBER: 118:73362
TITLE: Synthesis and ACE inhibitory activity of the stereoisomers of perindopril (S 9490) and perindoprilate (S 9780)
AUTHOR(S): Vincent, Michel; Marchand, Bernard; Remond, Georges; Jaguelin-Guinamant, Sylvie; Damien, Gerard; Portevin, Bernard; Baumal, Jean Yves; Volland, Jean Paul; Bouchet, Jean Paul; et al.
CORPORATE SOURCE: Inst. Rech. Serv. 11, Suresnes, 92150, Fr.
SOURCE: Drug Design and Discovery (1992), 9(1), 11-28
CODEN: DDDIEV; ISSN: 1055-9612
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

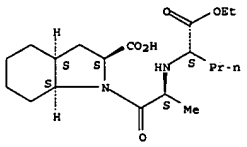


I, R=Et
II, R=H

AB Preindopril, a powerful ACE (angiotensin converting enzyme) inhibitor contains 5 chiral carbons, and thus there is the possibility of 25 = 32 stereoisomers for the general structure I. These 32 stereoisomers were prepared by crosscoupling the 8 stereoisomers of benzyl perhydroindole-2-carboxylate with the 4 stereoisomers of 2-(1-carbethoxybutylamino)propioni c acid, and hydrogenating the resulting benzyl esters. Each stereoisomer of perindopril furnished by saponification of the corresponding diacid stereoisomer (II) of perindoprilate which is the active form of perindopril. For each of the 32 stereoisomers of II, the in vitro ACE inhibitory potency was determined Four of them, including perindoprilate, had activities in the nanomolar range, and 4 more were ca. 10-fold less active. The 4 acid esters of I corresponding resp. to the 4 most active diacids II, in vitro were studied (1 mg/kg via the oral route) for their in vivo activity in dogs. The oral absorption of the active acid esters I and their activation to the active diacid II depended only on the chiralities of the 2 ring junction carbons of the perhydroindole ring.
IT 82834-16-0DP, Perindopril, isomers 82834-16-0P
145513-30-0P 145513-31-1P 145513-32-2P
145513-33-3P 145513-34-4P 145513-35-5P
145513-36-6P 145513-37-7P 145513-38-8P
145513-39-9P 145513-40-2P 145513-41-3P
145513-42-4P 145513-43-5P 145513-44-6P
145513-45-7P 145513-46-8P 145513-47-9P
145513-48-0P 145513-49-1P 145513-50-4P
145513-51-5P 145513-52-6P 145513-53-7P
145513-54-8P 145513-55-9P 145513-56-0P
145513-57-1P 145513-58-2P 145513-59-3P

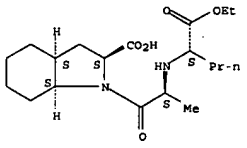
L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
145513-94-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and angiotensin I-converting enzyme inhibitory activity of, chirality-structure activity in relation to)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

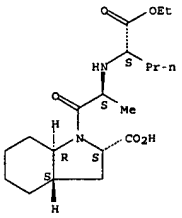
Absolute stereochemistry. Rotation (-).



RN 145513-30-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aβ,7aα]]- (9CI) (CA INDEX NAME)

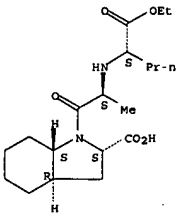
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-31-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aα,7aβ]]- (9CI) (CA INDEX NAME)

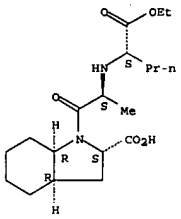
Absolute stereochemistry.



RN 145513-32-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aα,7aα]]- (9CI) (CA INDEX NAME)

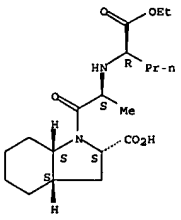
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-33-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

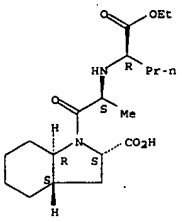
Absolute stereochemistry.



RN 145513-34-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3aβ,7aα]]- (9CI) (CA INDEX NAME)

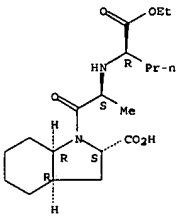
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-35-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3aα,7aα]]- (9CI)
(CA INDEX NAME)

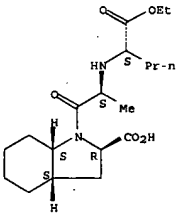
Absolute stereochemistry.



RN 145513-36-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

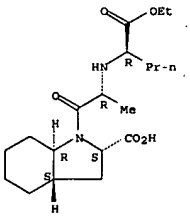
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-39-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(S*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

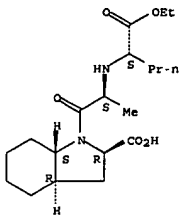
Absolute stereochemistry.



RN 145513-40-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(R*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

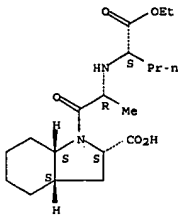
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-37-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2α,3aβ,7aβ]]- (9CI)
(CA INDEX NAME)

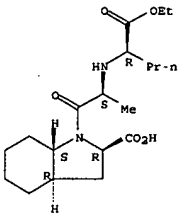
Absolute stereochemistry.



RN 145513-38-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2α,3aα,7aα]]- (9CI)
(CA INDEX NAME)

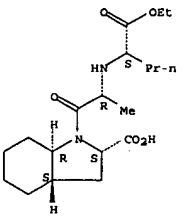
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-41-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

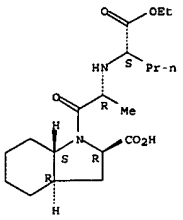
Absolute stereochemistry.



RN 145513-42-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(S*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

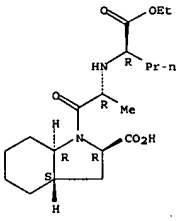
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-43-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(R*)],2α,3aα,7aβ]]- (9CI) (CA INDEX NAME)

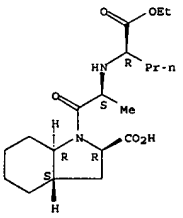
Absolute stereochemistry.



RN 145513-44-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(S*)],2α,3aα,7aα]]- (9CI) (CA INDEX NAME)

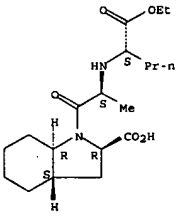
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-47-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2α,3aα,7aβ]]- (9CI) (CA INDEX NAME)

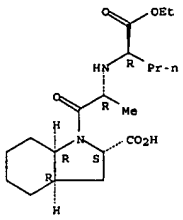
Absolute stereochemistry.



RN 145513-48-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2R)-2-[[(1R)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2R,3aR,7aR)- (9CI) (CA INDEX NAME)

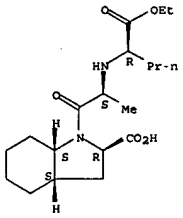
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-45-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(R*)],2α,3aα,7aα]]- (9CI) (CA INDEX NAME)

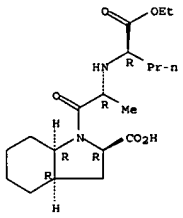
Absolute stereochemistry.



RN 145513-46-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(R*)],2α,3aα,7aβ]]- (9CI) (CA INDEX NAME)

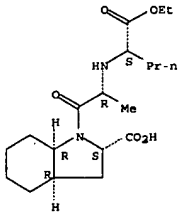
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-49-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2α,3aα,7aα]]- (9CI) (CA INDEX NAME)

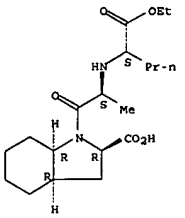
Absolute stereochemistry.



RN 145513-50-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

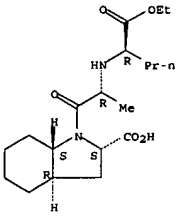
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-51-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(S*)],2α,3aα,7aβ]]- (9CI)
(CA INDEX NAME)

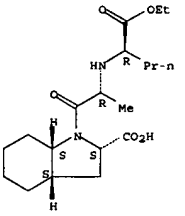
Absolute stereochemistry.



RN 145513-52-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(S*)],2α,3aβ,7aβ]]- (9CI)
(CA INDEX NAME)

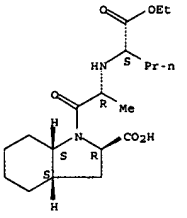
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-55-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2R)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2R,3aS,7aS)- (9CI)
(CA INDEX NAME)

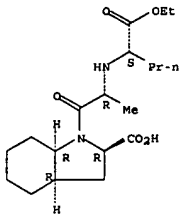
Absolute stereochemistry.



RN 145513-56-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(R*)],2α,3aβ,7aβ]]- (9CI)
(CA INDEX NAME)

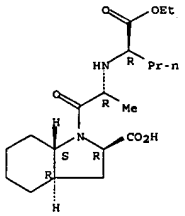
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-53-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(R*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

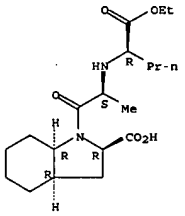
Absolute stereochemistry.



RN 145513-54-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(S*)],2α,3aβ,7aβ]]- (9CI)
(CA INDEX NAME)

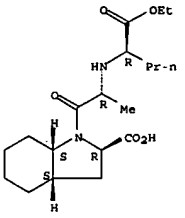
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-57-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(R*)],2α,3aα,7aα]]- (9CI)
(CA INDEX NAME)

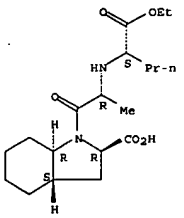
Absolute stereochemistry.



RN 145513-58-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(S*)],2α,3aα,7aβ]]- (9CI)
(CA INDEX NAME)

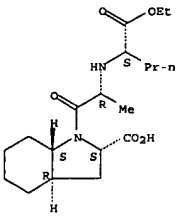
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 145513-59-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2α,3aα,7aβ]]- (9CI) (CA INDEX NAME)

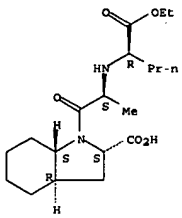
Absolute stereochemistry.



RN 145513-94-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3aα,7aβ]]- (9CI) (CA INDEX NAME)

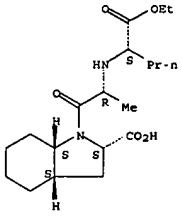
Absolute stereochemistry.

L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



IT 130982-52-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 130982-52-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2S-[1[S*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

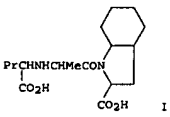
Absolute stereochemistry.



● HCl

L5 ANSWER 30 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:74706 CAPLUS
DOCUMENT NUMBER: 114:74706
TITLE: Configuration and preferential solid-state conformations of perindoprilat (S-9780). Comparison with the crystal structures of other ACE inhibitors and conclusions related to structure-activity relationships
AUTHOR(S): Pascard, Claudine; Guilhem, Jean; Vincent, Michel; Remond, Georges; Portevin, Bernard; Laubie, Michel
CORPORATE SOURCE: Inst. Chim. Subst. Nat., Gif-sur-Yvette, 91198, Fr.
SOURCE: Journal of Medicinal Chemistry (1991), 34(2), 663-9
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

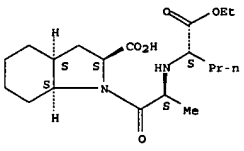


I

AB The conformational of perindoprilat (I), an antihypertensive drug, is studied in the solid state by X-ray anal. The resolution of its structure reveals important analogies between its observed conformation and that of several angiotensin-converting enzyme (ACE) inhibitors of the same family. This comparison points out a constant relative orientation of the functional groups, regardless of the mol. environment. This angular constancy appears not to be accidental and is a good argument for the spatial design of the ACE binding site. Although ACE is a carboxydipeptidase, the binding site may not contain two but one unique hydrophobic pocket receiving the C-terminal end of the inhibitors.
IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(saponification of)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 30 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L5 ANSWER 31 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:478983 CAPLUS
DOCUMENT NUMBER: 113:78983
TITLE: Preparation of N-(carboxyalkyl)dipeptides as antiglaucoma agents
INVENTOR(S): Andrews, David R.; Gaeta, Federico C. A.; Watkins, Robert W.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: U.S., 24 pp. Cont.-in-part of U.S. Ser. No. 784,000.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4885293	A	19891205	US 1986-892003	19860730
US 4556655	A	19851203	US 1984-653186	19840924
US 4634698	A	19870106	US 1985-721015	19850408
US 4826816	A	19890502	US 1985-784000	19851004
US 5015641	A	19910514	US 1989-349369	19890509
PRIORITY APPLN. INFO.:			US 1984-653186	A2 19840924
			US 1985-721015	A2 19850408
			US 1985-784000	A2 19851004
			US 1986-892003	A3 19860730

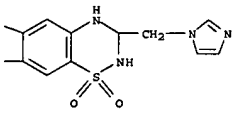
OTHER SOURCE(S): CASREACT 113:78983; MARPAT 113:78983
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

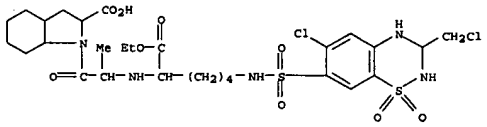
AB DSO2NR1BCH(COR6)ECHR7COACOR8 [I; A = Q, Q1, etc.; p, q = 0-2; B = JLM; J = (CH2)s, (CH2)lW; L = bond, cis- or trans-alkenylene, alkynylene, ZZ1, Z1Z, ZZ2, Z2Z, (un)substituted 5- or 6-membered heterocyclic radical containing 3-5 C atoms and 1 or 2 of N, O, S; M = (CH2)u, (CH2)tX(CH2)v; s, u, v = 0-5; t = 1-5; D = benzothiadiazinyl moiety Q2; E = O, S, NH, CH2; W = CONH, NHCO; X, Z = bond, O, S, (un)substituted NH; Z1 = (un)substituted 1,2-, 1,3-, or 1,4-phenylene; Z2 = (un)substituted 1,2-, 1,3- or 1,4-cycloalkanediyl; R6, R8 = HO, C1-8 alkoxy, PhCH2, allyl, etc.; R7 = H, (amino)alkyl], useful for reducing and controlling elevated intraocular pressure (no data), were prepared Thus, condensation of L-serine derivative II (R9 = Me3CO, R10 = H)

L5 ANSWER 31 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-B

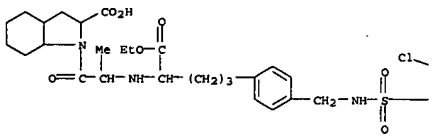


L5 ANSWER 31 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(prepn. given) with a benzothiadiazinesulfonyl chloride deriv. Q3Cl in THF contg. (Me2CH)2NEt and deprotection of the product with HCl/dioxane gave II (R9 = HO, R10 = Q3) which was then condensed with cis,syn-octahydroindole-2(S)-carboxylic acid tert-Bu ester (prepn. given) in DMF contg. 1-hydroxybenzotriazole and Me2N(CH2)3N:C:NEt.HCl followed by deprotection with HCl/dioxane, to give II [R9 = cis,syn-2(S)-Q4, R10 = unchanged]..
IT 109854-18-4P 128529-20-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for treatment of glaucoma)
RN 109854-18-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[[6-chloro-3-(chloromethyl)-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl]sulfonyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



RN 128529-20-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-[4-[[[[6-chloro-3,4-dihydro-3-(1H-imidazol-1-ylmethyl)-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl]sulfonyl]amino]methyl]phenyl]-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

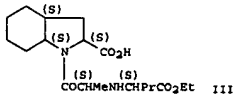
PAGE 1-A



L5 ANSWER 32 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:534746 CAPLUS
DOCUMENT NUMBER: 111:134746
TITLE: Preparation of N-[(alkoxycarbonyl)alkyl]-L-alanines as intermediates for carboxyalkyl dipeptides
INVENTOR(S): Vincent, Michel; Beliarda, Jean; Marchand, Bernard; Remond, Georges
PATENT ASSIGNEE(S): ADIR, Fr.
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 308340	A1	19890322	EP 1988-402338	19880916
EP 308340	B1	19910313		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620699	A1	19890324	FR 1987-12901	19870917
FR 2620699	B1	19900601		
CA 1340570	A1	19990601	CA 1988-577077	19880907
DK 8805150	A	19890318	DK 1988-5150	19880915
DK 172005	B1	19970915		
AU 8822355	A1	19890323	AU 1988-22355	19880916
AU 606992	B2	19910221		
JP 01110652	A2	19890427	JP 1988-232124	19880916
JP 06099373	B4	19941207		
ZA 8806930	A	19890530	ZA 1988-6930	19880916
US 4902817	A	19900220	US 1988-245353	19880916
AT 61566	E	19910315	AT 1988-402338	19880916
ES 2033451	T3	19930316	ES 1988-402338	19880916
PRIORITY APPLN. INFO.:			FR 1987-12901	A 19870917
			EP 1988-402338	A 19880916

OTHER SOURCE(S): CASREACT 111:134746; MARPAT 111:134746
GI

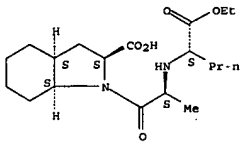


III

AB The title compds., (S,S)-HO2CCHMeNHCHR1CO2R2 (I; R1 = alkyl; R2 = H, alkyl), useful as intermediates for carboxyalkyl dipeptides R3CO-Q-COCHMeNHCHR2 (II; R3 = H, alkyl; Q = a residue of indoline, isoindoline, tetrahydroquinoline, perhydroindole, perhydroisoindole, perhydroisoquinoline, etc.), notably perindopril (III), an antihypertensive, are prepared via esterification of (S)-H2NCHR1CO2H (IV) with R2OH and reaction of the resulting (S)-H2NCHR1CO2R2 with pyruvic acid

L5 ANSWER 32 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
under catalytic hydrogenation conditions. (S)-H2NCHPrCO2Et (prepn. given) was reacted with pyruvic acid under hydrogenation in the presence of Pd/C to give (S,S)-HO2CCHMeNHCHPrCO2Et.
IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediate for, N-[(ethoxycarbonyl)butyl]alanine as)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

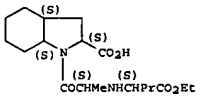


L5 ANSWER 33 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:515749 CAPLUS
DOCUMENT NUMBER: 111:115749
TITLE: Preparation of perindopril via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine
INVENTOR(S): Vincent, Michel; Baliarda, Jean; Marchand, Bernard; Remond, Georges
PATENT ASSIGNEE(S): ADIR, Fr.
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

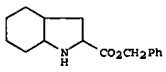
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 308341	A1	19890322	EP 1988-402339	19880916
EP 308341	B1	19901212		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620709	A1	19890324	FR 1987-12896	19870917
FR 2620709	B1	19900907		
CA 1336348	A1	19950718	CA 1988-577078	19880907
DK 8805151	A	19890318	DK 1988-5151	19880915
DK 171470	B1	19961111		
AU 8822362	A1	19890323	AU 1988-22362	19880916
AU 608363	B2	19910328		
JP 01110696	A2	19890427	JP 1988-232125	19880916
JP 05043717	B4	19930702		
ZA 8806932	A	19890530	ZA 1988-6932	19880916
US 4914214	A	19900403	US 1988-245446	19880916
AT 59047	E	19901215	AT 1988-402339	19880916
CA 1338015	A1	19960130	CA 1991-616239	19911128

PRIORITY APPLN. INFO.:
FR 1987-12896 A 19870917
CA 1988-577078 A3 19880907
EP 1988-402339 A 19880916

OTHER SOURCE(S): MARPAT 111:115749
GI



I



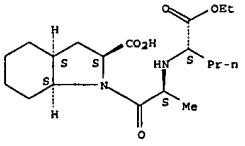
II

L5 ANSWER 33 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
AB Preparation of perindopril via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine. The title compound (I), useful as an antihypertensive (no data), is prepared, e.g., via N-acylation of perhydroindole derivative II (preparation given) with (S,S)-HO2CCHMeNHCHPrCO2Et (III). II.p-MeC6H4SO3H (preparation given) was condensed with III in EtOAc containing Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to give, after deprotection and treatment with Me3CNH2, I.Me3CNH2.
IT 107133-36-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via acylation of perhydroindole derivative with N-[(ethoxycarbonyl)butyl]alanine)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



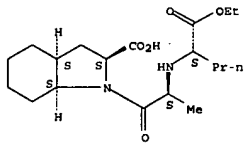
CM 2

CRN 75-64-9
CMF C4 H11 N

IT 82834-16-0P, Perindopril
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine)
RN 82834-16-0 CAPLUS

L5 ANSWER 33 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

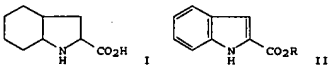


L5 ANSWER 34 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:477846 CAPLUS
DOCUMENT NUMBER: 111:77846
TITLE: Industrial preparation of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid as intermediate for antihypertensive perindopril
INVENTOR(S): Vincent, Michel; Baliarda, Jean; Marchand, Bernard; Remond, Georges
PATENT ASSIGNEE(S): ADIR, Pr.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 308339	A1	19890322	EP 1988-402337	19880916
EP 308339	B1	19920506		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620703	A1	19890324	FR 1987-12900	19870917
FR 2620703	B1	19911004		
DK 8805149	A	19890318	DK 1988-5149	19880915
AU 8822361	A1	19890323	AU 1988-22361	19880916
AU 618752	B2	19920109		
ZA 8806931	A	19890530	ZA 1988-6931	19880916
US 4935525	A	19900619	US 1988-245352	19880916
JP 02191251	A2	19900727	JP 1988-232123	19880916
AT 75735	E	19920515	AT 1988-402337	19880916
ES 2033450	T3	19930316	ES 1988-402337	19880916
US 4954640	A	19900904	US 1990-462797	19900110

PRIORITY APPLN. INFO.: FR 1987-12900 A 19870917
EP 1988-402337 A 19880916
US 1988-245352 A3 19880916

OTHER SOURCE(S): CASREACT 111:77846; MARPAT 111:77846
GI

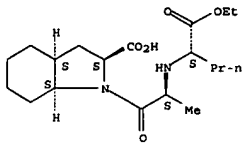


AB The title compound (I), useful as an intermediate for antihypertensive perindopril, was prepared from indolecarboxylic acid deriva. II (R = H, lower alkyl). Esterification of II (R = H) in EtOH containing H_2SO_4, reduction

L5 ANSWER 34 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L5 ANSWER 34 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
with Sn in EtOH contg. HCl, sapon., and resoln. gave (S)-indoline-2-carboxylic acid (III). Hydrogenation of III over Rh under H2 at 60° gave (2S,3aS,7aS)-octahydroindole-2-carboxylic acid.
IT 82834-16-0 107133-36-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediate for, octahydroindolecarboxylic acid as)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

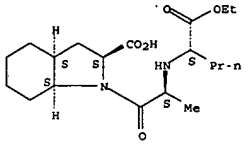


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

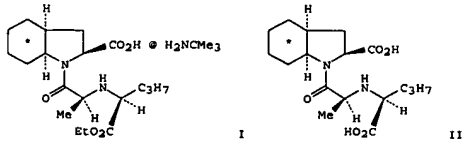
Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L5 ANSWER 35 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:631529 CAPLUS
DOCUMENT NUMBER: 109:231529
TITLE: Synthesis of S9490-3 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-(ethoxycarbonylbutyl)amino]-1-oxopropyl]-(2S,3aS,7aS)-perhydroindole-2-carboxylic acid tert-butylamine salt and S9780 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-(carboxybutyl)amino]-1-oxopropyl]-2S,3aS,7aS)-perhydroindole-2-carboxylic acid and of [3,4-3H-butylamino]S9490-3 and [(3,4-3H-)butylamino]S9780
AUTHOR(S): Pichat, L.; Tostain, J.; Gomis, J. M.; Coppo, M.; Moustier, A. M.; Vincent, M.; Remond, G.; Portevin, B.; Laubie, M.
CORPORATE SOURCE: CEN Saclay, Gif sur Yvette, 91191, Fr.
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(5), 553-68
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: French
OTHER SOURCE(S): CASREACT 109:231529
GI



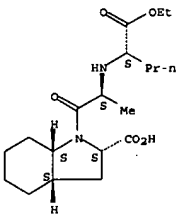
AB The title 14C-labeled compds. I (* signifies the uniform labeling of the cyclohexane ring with 14C) and II were prepared from aniline-U-14C in several steps. The title 3H-labeled compds. were also prepared The latter synthesis involved the tritiation of an allylglycine residue. The title compds. are potent inhibitors of angiotensin-converting enzyme.
IT 117770-49-7P 117770-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)
RN 117770-49-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, labeled with carbon-14, [2S-[1[R*(R*)],2α,3aα,7aβ]]-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 117770-48-6
CMF C19 H32 N2 O5
CIL XC-14

L5 ANSWER 35 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

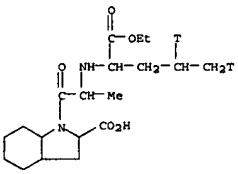
Absolute stereochemistry.



CM 2

CRN 75-64-9
CMF C4 H11 N

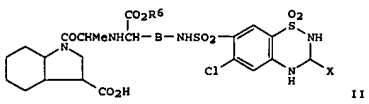
RN 117770-64-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl-3,4-t2]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



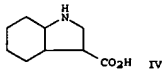
L5 ANSWER 36 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:22286 CAPLUS
DOCUMENT NUMBER: 108:22286
TITLE: Preparation of peptides as antiglaucoma agents
INVENTOR(S): Andrews, David R.; Gaeta, Federico C. A.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: U.S., 15 pp. Cont.-in-part of U.S. 4,556,655.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4634698	A	19870106	US 1985-721015	19850408
US 4556655	A	19851203	US 1984-653186	19840924
US 4826816	A	19890502	US 1985-784000	19851004
US 4885293	A	19891205	US 1986-892003	19860730
US 5015641	A	19910514	US 1989-349369	19890509
PRIORITY APPLN. INFO.:			US 1984-653186	A2 19840924
			US 1985-721015	A2 19850408
			US 1985-784000	A2 19851004
			US 1986-892003	A3 19860730

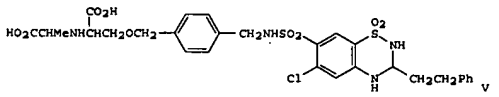
OTHER SOURCE(S): CASREACT 108:22286
GI



II



IV



V

AB D-SO2NR1-B-CH(COR6)-E-CHR7-CO-A-COR8 [I; A = heterocycle residue, e.g., 1,2-pyrrolidinediyl, 1,2-perhydroindolediyl; B = (substituted)

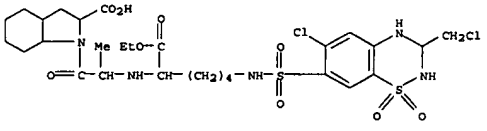
L5 ANSWER 35 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L5 ANSWER 36 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

residue, e.g., (CH2)4; D-substituted S,S-dioxo-3,4-dihydro-1,2,4-benzothiadiazin-7-yl; E = NH, O, S, CH2], e.g., II [R6 = H, B = (CH2)4, X = CH2Cl] (III), useful for reducing intraocular pressure, are prepd. Dipeptide II (R6 = Et, B = p-CH2OCH2C6H4CH2, X = CH2CH2Ph) was prepd. in many steps via alkylation of indole deriv. IV with alanine deriv. V followed by hydrogenolysis. An antiglaucoma compn. (1 mL) (adjusted to pH 7.4 with 1N NaOH) for topical use contained III 10.0, NaH2PO4 10.4, Na2HPO4 2.4, chlorobutanol 5.0, hydroxypropyl methylcellulose 5.0 g, and water.

IT 109854-18-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antiglaucoma agent)

RN 109854-18-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[[6-chloro-3-(chloromethyl)-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl]sulfonyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



L5 ANSWER 37 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:497126 CAPLUS
DOCUMENT NUMBER: 107:97126
TITLE: Dipeptide derivatives containing sulfoamide group as antihypertensives having both diuretic and angiotensin converting enzyme inhibitory activity
INVENTOR(S): Andrews, David R.; Gaeta, Federico C. A.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: U.S., 16 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

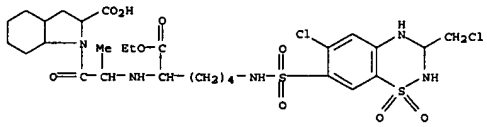
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4556655	A	19851203	US 1984-653186	19840924
US 4634698	A	19870106	US 1985-721015	19850408
WO 8601803	A1	19860327	WO 1985-US1778	19850919
W: AU, DK, JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8549639	A1	19860408	AU 1985-49639	19850919
AU 581388	B2	19890216		
EP 195817	A1	19861001	EP 1985-905015	19850919
EP 195817	B1	19891018		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 62500241	T2	19870129	JP 1985-504453	19850919
AT 47399	E	19891115	AT 1985-905015	19850919
ZA 8507358	A	19860528	ZA 1985-7358	19850924
IL 76484	A1	19900209	IL 1985-76484	19850924
CA 1278150	A1	19901218	CA 1985-491447	19850924
US 4826816	A	19890502	US 1985-784000	19851004
DK 8602416	A	19860523	DK 1986-2416	19860523
US 4885293	A	19891205	US 1986-892003	19860730
US 5015641	A	19910514	US 1989-349369	19890509

PRIORITY APPLN. INFO.:

US 1984-653186	A2	19840924
US 1985-721015	A2	19850408
EP 1985-905015	A	19850919
WO 1985-US1778	A	19850919
US 1985-784000	A2	19851004
US 1986-892003	A3	19860730

OTHER SOURCE(S): CASREACT 107:97126; MARPAT 107:97126
AB The title compds. useful in treatment of hypertension and glaucoma (no data) were prepared 1-[2-(S)-[[1-(S)-Carboxy-2-[4-[[[6-chloro-3,4-dihydro-3-(2-phenylethyl)-2H-1,2,4-benzothiadiazin-7-yl]sulfonylamino]methyl]phenylmethoxy]ethyl]amino]-1-oxopropyl]-(2S,3α,7aα)-octahydro-1H-

L5 ANSWER 37 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
indole-2-carboxylic acid S,S-dioxide prepd. in 8 steps from N-tert-butoxycarbonyl-L-serine, was used in formulation of a capsule, tablet, and injectable soln.
IT 109854-18-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)
RN 109854-18-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[[6-chloro-3-(chloromethyl)-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl]sulfonyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



L5 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:175294 CAPLUS
DOCUMENT NUMBER: 100:175294
TITLE: Carboxyalkyl dipeptides and pharmaceutical compositions containing them
INVENTOR(S): Smith, Elizabeth M.; Witkowski, Joseph T.; Doll, Ronald J.; Gold, Elijah H.; Neustadt, Bernard R.; Yehaskel, Albert S.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: Eur. Pat. Appl., 134 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 88350	A1	19830914	EP 1983-102014	19830302
EP 88350	B1	19850220		
R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE				
US 4431644	A	19840214	US 1982-355638	19820308
US 4431645	A	19840214	US 1982-355639	19820308
ZA 8300362	A	19840926	ZA 1983-362	19830119
AT 11921	E	19850315	AT 1983-102014	19830302
NO 8300737	A	19830909	NO 1983-737	19830303
AU 8312035	A1	19830915	AU 1983-12035	19830303
AU 557795	B2	19870108		
GB 2117777	A1	19831019	GB 1983-5837	19830303
GB 2117777	B2	19850626		
ES 520261	A1	19840401	ES 1983-520261	19830303
DK 8301101	A	19830909	DK 1983-1101	19830304
JP 58162561	A2	19830927	JP 1983-35707	19830304
FI 8300752	A	19830909	FI 1983-752	19830307
HU 29605	O	19840228	HU 1983-781	19830307
HU 195520	B	19880530		
ZA 8301844	A	19840627	ZA 1983-1844	19830316

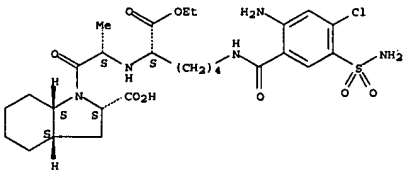
PRIORITY APPLN. INFO.:

US 1982-355638	A	19820308
US 1982-355639	A	19820308
US 1982-360532	A	19820322
ZA 1983-362	A	19830119
EP 1983-102014	A	19830302

OTHER SOURCE(S): CASREACT 100:175294; MARPAT 100:175294
GI For diagram(s), see printed CA Issue.
AB Title compds. RCH2CR1(CO2H)-NHCH[(CH2)nXR2]CO-X1-OH [R = alkyl, PhCH2, PhCH2O, PhCH2S, PhO, PhS; R1 = H, alkyl; X = S, R2 = substituted (3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazin-3-yl 1,1-dioxide) methyl; X = NR3 (R3 = H, alkyl, Ph), R2 = sulfamoyl-substituted Bz, PhSO2, or benzyl; XR2 = sulfamoyl-substituted N-containing heterocyclic ring; n = 1-6; X1 = (un)substituted Pro or related N-containing heterocyclic amino acid residues] were prepared as antihypertensives and agents for the treatment of congestive heart failure and glaucoma (no data). Thus, H-L-Lys(Z)-OH (Z

L5 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CO2CH2Ph) was treated with PhCH2CH2COCO2Et and NaBH3CN to give (S)-PhCH2CH2CH(CO2Et)-L-Lys(Z)-OH, which was condensed with indole I to give dipeptide II (R4 = Z, R5 = CH2Ph), which was deblocked by hydrogenolysis to give II (R4 = R5 = H), which was sulfonylated with 4-chloro-3-sulfamoylbenzenesulfonyl chloride to give title compd. III.
IT 89083-71-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation of, with benzaldehyde)
RN 89083-71-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[2-amino-5-(aminosulfonyl)-4-chlorobenzoyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro-, hydrochloride, [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

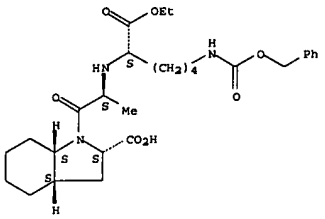


●x HCl

IT 89083-56-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)
RN 89083-56-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-5-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

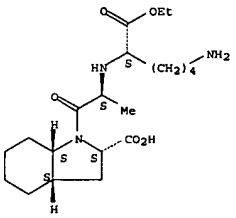
Absolute stereochemistry.

L5 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



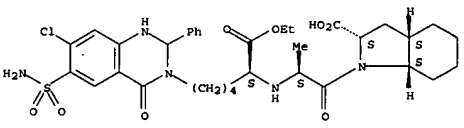
IT 89083-57-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfonylation of)
RN 89083-57-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-amino-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 89083-58-9P 89083-59-0P 89091-48-5P
89105-59-9P 89105-62-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 89083-58-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[[3-(aminosulfonyl)-4-chlorophenyl]sulfonyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

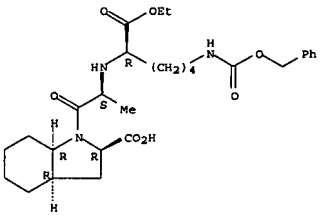
L5 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



●x HCl

RN 89105-59-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-5-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1-oxopropyl]octahydro-, [1[S*(R*)],2α,3aβ,7aβ]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

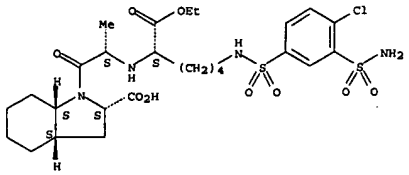


RN 89105-62-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[3-(aminosulfonyl)-4-chlorobenzoyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

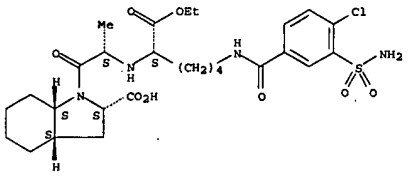
L5 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



RN 89083-59-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[3-(aminosulfonyl)-4-chlorobenzoyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

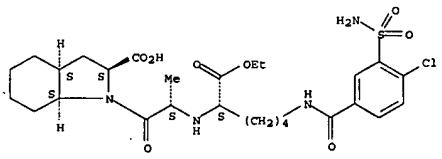
Absolute stereochemistry.



RN 89091-48-5 CAPLUS
CN 3(2H)-Quinazolinehexanoic acid, 6-(aminosulfonyl)-α-[[2-(2-carboxyoctahydro-1H-indol-1-yl)-1-methyl-2-oxoethyl]amino]-7-chloro-1,4-dihydro-4-oxo-2-phenyl-, monoethyl ester, hydrochloride, [1[R*(R*)],2α,3aβ,7aβ]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L5 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



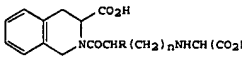
● HCl

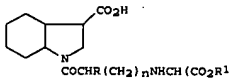
L5 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:616716 CAPLUS
DOCUMENT NUMBER: 97:216716
TITLE: Substituted imino diacids and pharmaceutical preparations containing them
INVENTOR(S): Remond, Georges; Laubie, Michel; Vincent, Michel
PATENT ASSIGNEE(S): Science Union et Cie., Societe Francaise de Recherche Medicale, Fr.
SOURCE: Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

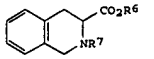
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 49658	A1	19820414	EP 1981-401501	19810929
EP 49658	B1	19840613		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
FR 2491469	A1	19820409	FR 1980-21095	19801002
FR 2491469	B1	19830513		
FR 2503155	A2	19821008	FR 1981-6916	19810407
FR 2503155	B2	19830701		
IL 63940	A1	19850630	IL 1981-63940	19810925
AT 7910	E	19840615	AT 1981-401501	19810929
FI 8103034	A	19820403	FI 1981-3034	19810930
FI 77230	B	19881031		
FI 77230	C	19890210		
DK 8104343	A	19820403	DK 1981-4343	19811001
DK 157011	B	19891030		
DK 157011	C	19900326		
NO 8103339	A	19820405	NO 1981-3339	19811001
NO 160780	B	19890220		
NO 160780	C	19890531		
AU 8175949	A1	19820408	AU 1981-75949	19811001
AU 542611	B2	19850228		
HU 28405	O	19831228	HU 1981-2838	19811001
HU 185147	B	19841228		
SU 1153827	A3	19850430	SU 1981-3344196	19811001
CA 1341196	A1	20010306	CA 1981-387093	19811001
JP 57091974	A2	19820608	JP 1981-157367	19811002
JP 01032239	B4	19890629		
ZA 8106844	A	19820929	ZA 1981-6844	19811002
ES 505999	A1	19830416	ES 1981-505999	19811002
US 4508729	A	19850402	US 1981-308234	19811002
US 4565819	A	19860121	US 1982-420005	19820920
US 4616029	A	19861007	US 1984-659275	19841010
US 4616031	A	19861007	US 1984-659276	19841010
US 4644008	A	19870217	US 1984-659274	19841010
US 4616030	A	19861007	US 1984-679320	19841206

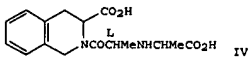
PRIORITY APPLN. INFO.: FR 1980-21095 A 19801002
FR 1981-6916 A 19810407
FR 1979-30046 A 19791207
FR 1980-16875 A 19800731
US 1980-212607 A2 19801203
EP 1981-401501 A 19810929
US 1981-308234 A1 19811002

OTHER SOURCE(S): CASREACT 97:216716; MARPAT 97:216716
GI


I


II


III


IV

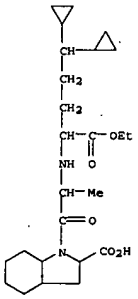
AB Heterocyclic amino acid derivs. I and II [R = C1-4 alkyl; R1 = H, C1-4 alkyl; R2 = alkyl, mono- or dicycloalkylalkyl, phenylalkyl, (CH2)mXCHR3R4 [R3 = H, C1-4 alkyl, C3-6 cycloalkyl; R4 = H, C1-4 alkyl, C3-6 cycloalkyl, alkoxycarbonyl; X = S, NR5 (R5 = H, Ac, CO2CH2Ph), m = 1, 2]; n = 0, 1] were prepared Thus, (S)-phenylalanine was cyclized with H2CO to give (S)-isoquinoline (S)-III (R6 = R7 = H), which was esterified with MeOH/SOCl2 and then condensed with Boc-L-Ala-OH (Boc = Me3CO2C) by DCC/1-hydroxybenzotriazole to give (S)-III (R6 = Me, R7 = Boc-L-Ala). The latter was saponified and then Boc-deblocked by CF3CO2H to give (S)-III.CF3CO2H (R6 = H, R7 = H-L-Ala), which was treated with MeCOCO2H and then reduced by NaBH3CN to give isoquinoline (2S)-IV. I and II were useful as therapeutic agents due to their ability to inhibit enkephalinase, carboxypolypeptidase, kininase, and angiotensin-converting enzyme (ACE); e.g., the compds. can be used as antihypertensives since they inhibit ACE.

IT 82961-95-3P 82962-01-4P 82962-05-8P
82962-10-5P 82962-11-6P 82962-14-9P
82975-58-4P 82978-68-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L5 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 82961-95-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4,4-dicyclopropyl-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

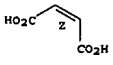
CRN 82961-94-2
CMF C25 H40 N2 O5



CM 2

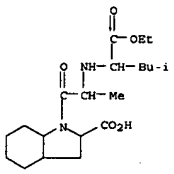
CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



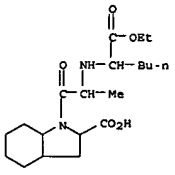
RN 82962-01-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-methylbutyl]amino]-1-oxopropyl]octahydro-, monosodium salt (9CI) (CA INDEX NAME)

L5 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● Na

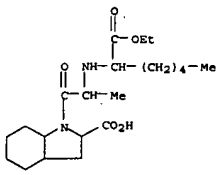
RN 82962-05-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro-, monosodium salt (9CI) (CA INDEX NAME)



● Na

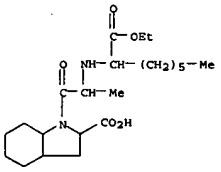
RN 82962-10-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)hexyl]amino]-1-oxopropyl]octahydro-, monosodium salt (9CI) (CA INDEX NAME)

L5 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● Na

RN 82962-11-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)heptyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



RN 82962-14-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)nonyl]amino]-1-oxopropyl]octahydro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

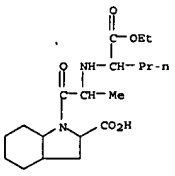
CRN 82962-13-8
CMF C24 H42 N2 O5

L5 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

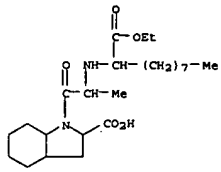
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 82978-68-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



L5 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



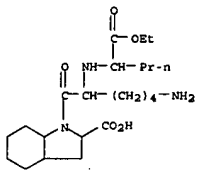
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 82975-58-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[6-amino-2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxohexyl]octahydro-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

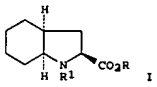
CM 1

CRN 82975-57-3
CMF C22 H39 N3 O5



L5 ANSWER 40 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1982:510360 CAPLUS
DOCUMENT NUMBER: 97:110360
TITLE: Stereoselective synthesis of a new perhydroindole derivative of chiral iminodiacid, a potent inhibitor of angiotensin converting enzyme
AUTHOR(S): Vincent, M.; Remond, G.; Portevin, B.; Serkiz, B.; Laubie, M.
CORPORATE SOURCE: Inst. Rech. Servier, Suresnes, 92150, Fr.
SOURCE: Tetrahedron Letters (1982), 23(16), 1677-80
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

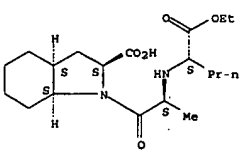


AB The title enzyme inhibitor I (R = H, R1 = S,S-COCHMeNHCHPrCO2Et) (II) was prepared by coupling reaction of I (R = CMe3, R1 = H) (III) with (S,S)-HO2CCHMeN+H2CHPrCO2Et Cl- (IV). III was stereospecifically prepared from (S)-2-carboxyindoline in 5 steps; IV was stereoselectively prepared by reaction of PrCOCO2Et with (S)-H2NCHMeCO2CMe3 or by reaction of (S)-PrCH(CO2Et)N+H3 Cl- with MeCOCO2H. II showed 40% angiotensin converting enzyme inhibition after 24-30 h in dogs treated with 1 mg/kg p.o.

IT 82834-16-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and angiotensin converting enzyme inhibition by)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



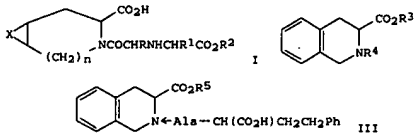
L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:492759 CAPLUS
DOCUMENT NUMBER: 97:92759
TITLE: Amino acid derivatives, compositions containing them and their use
INVENTOR(S): Geiger, Rolf; Teetz, Volker; Urbach, Hansjoerg; Schoelkens, Bernward; Henning, Rainer
PATENT ASSIGNEE(S): Hoechst A.-G. , Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 196 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 46953	A2	19820310	EP 1981-106535	19810822
EP 46953	A3	19820505		
EP 46953	B1	19891206		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
DE 3032709	A1	19820429	DE 1980-3032709	19800830
DE 3118191	A1	19821125	DE 1981-3118191	19810508
EP 278530	A2	19880817	EP 1988-102408	19810822
EP 278530	A3	19890802		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
EP 328160	A1	19890816	EP 1989-105371	19810822
EP 328160	B1	19940504		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 48415	E	19891215	AT 1981-106535	19810822
AT 105301	E	19940515	AT 1989-105371	19810822
ES 504955	A1	19820816	ES 1981-504955	19810825
FI 8102652	A	19820301	FI 1981-2652	19810827
FI 90072	B	19930915		
FI 90072	C	19931227		
HU 27874	O	19831128	HU 1981-2478	19810827
HU 189531	B	19860728		
DK 8103835	A	19820301	DK 1981-3835	19810828
DK 169382	B1	19941017		
NO 8102933	A	19820301	NO 1981-2933	19810828
AU 8174718	A1	19820311	AU 1981-74718	19810828
AU 544756	B2	19850613		
ZA 8105988	A	19820825	ZA 1981-5988	19810828
IL 63683	A1	19880331	IL 1981-63683	19810828
JP 01048918	B4	19891020	JP 1981-134401	19810828
ES 505604	A1	19821116	ES 1981-505604	19810918
ES 505605	A1	19821116	ES 1981-505605	19810918
US 5158959	A	19921027	US 1983-565900	19831227
US 5162362	A	19921110	US 1983-565887	19831227
AU 8779284	A1	19880204	AU 1987-79284	19871001
AU 599151	B2	19900712		
JP 01125398	A2	19890517	JP 1988-209625	19880825
JP 06078355	B4	19941005		
AU 8936625	A1	19891005	AU 1989-36625	19890620
AU 627741	B2	19920903		
JP 04217994	A2	19920807	JP 1991-77208	19910318
JP 07121955	B4	19951225		
FI 90069	B	19930915	FI 1991-4555	19910927
FI 90069	C	19931227		
FI 90532	B	19931115	FI 1991-4554	19910927
FI 90532	C	19940225		
US 5401766	A	19950328	US 1994-208443	19940309

PRIORITY APPLN. INFO.:

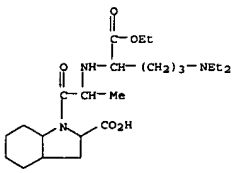
DE 1980-3032709	A	19800830
DE 1981-3118191	A	19810508
EP 1981-106535	P	19810822
EP 1989-105371	A	19810822
US 1981-297191	A3	19810828

OTHER SOURCE(S): CASREACT 97:92759; MARPAT 97:92759
GI

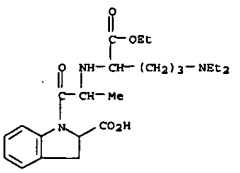


AB Amino acid derivs. I (X = fused benzene or cyclohexane ring; R, R1 = alkyl, alkenyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl, aryl, partially hydrogenated aryl, aralkyl, heterocyclic residue; R2 = H, alkyl, alkenyl, aralkyl; n= 0, 1) were prepared as long-lasting antihypertensives (no data).
Thus, tetrahydroisoquinoline II (R3 = R4 = H) was treated with ZCl (Z = PhCH2O2C) to give II (R3 = H, R4 = Z), which was esterified with Me3COH by DCC in CH2Cl2 containing 4-(dimethylamino)pyridine to give 97% II (R3 = CMe3, R4 = Z), which was Z-deblocked by hydrogenolysis and then condensed with Z-Ala-OH by DCC/1-hydroxybenzotriazole to give II (R3 = CMe3, R4 = Z-Ala).
The latter was Z-deblocked by hydrogenolysis to give II (R = CMe3, R4 = Ala), which condensed with PhCH2CH2COCO2H and was then reduced with NaBH3CN to give isoquinoline III (R5 = CMe3), which was debutylated by CF3CO2H to give III (R5 = H).
IT 82705-52-0P 82711-01-1P 82713-42-6P
82713-43-7P 82713-44-8P 82713-45-9P
82713-47-1P 82713-48-2P 82713-49-3P

L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
82713-50-6P 82714-14-5P 82714-15-6P
82715-91-1P 82715-92-2P 82715-93-3P
82715-94-4P 82715-96-6P 82715-97-7P
82715-98-8P 82715-99-9P 82716-65-2P
82716-66-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 82705-52-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-(diethylamino)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



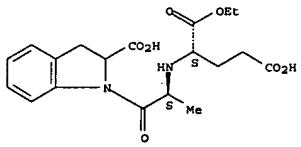
RN 82711-01-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-(diethylamino)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



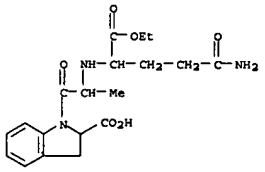
RN 82713-42-6 CAPLUS
CN L-Glutamic acid, N-[2-(2-carboxy-2,3-dihydro-1H-indol-1-yl)-1-methyl-2-oxoethyl]-, 1-ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

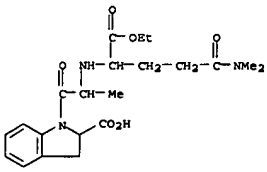
L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 82713-43-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-amino-1-(ethoxycarbonyl)-4-oxobutyl]amino]-1-oxopropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

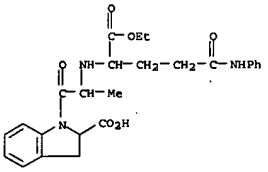


RN 82713-44-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-(dimethylamino)-1-(ethoxycarbonyl)-4-oxobutyl]amino]-1-oxopropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



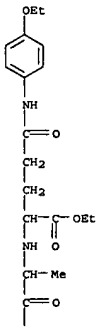
RN 82713-45-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-4-oxo-4-(phenylamino)butyl]amino]-1-oxopropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



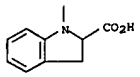
RN 82713-47-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-4-[(4-ethoxyphenyl)amino]-4-oxobutyl]amino]-1-oxopropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

PAGE 1-A

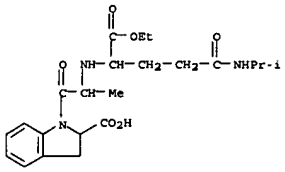


L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

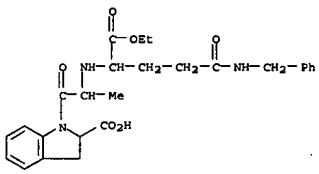
PAGE 2-A



RN 82713-48-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-4-[(1-methylethyl)amino]-4-oxobutyl]amino]-1-oxopropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



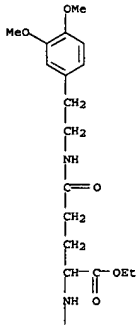
RN 82713-49-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-4-oxo-4-[(phenylmethyl)amino]butyl]amino]-1-oxopropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



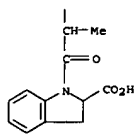
RN 82713-50-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-[[2-(3,4-dimethoxyphenyl)ethyl]amino]-1-(ethoxycarbonyl)-4-oxobutyl]amino]-1-oxopropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A

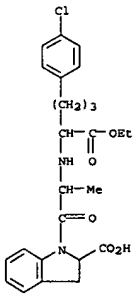


PAGE 2-A



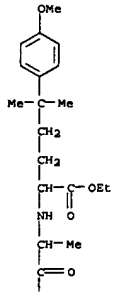
RN 82714-14-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-(4-chlorophenyl)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



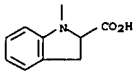
RN 82714-15-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-4-(4-methoxyphenyl)-4-methylpentyl]amino]-1-oxopropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

PAGE 1-A

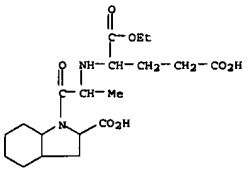


L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

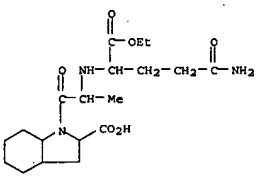
PAGE 2-A



RN 82715-91-1 CAPLUS
CN L-Glutamic acid, N-[2-(2-carboxyoctahydro-1H-indol-1-yl)-1-methyl-2-oxoethyl]-, 1-ethyl ester (9CI) (CA INDEX NAME)



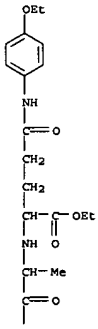
RN 82715-92-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-amino-1-(ethoxycarbonyl)-4-oxobutyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



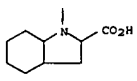
RN 82715-93-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-(dimethylamino)-1-(ethoxycarbonyl)-4-oxobutyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

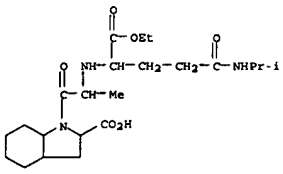
PAGE 1-A



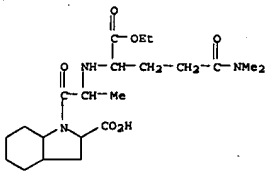
PAGE 2-A



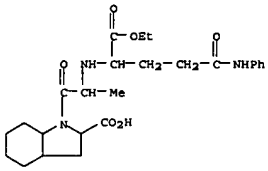
RN 82715-97-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-4-[(1-methylethyl)amino]-4-oxobutyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

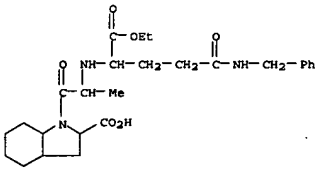


RN 82715-94-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-4-oxo-4-(phenylamino)butyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



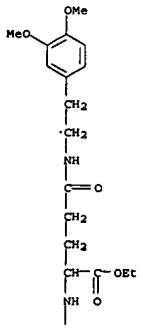
RN 82715-96-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-4-[(4-ethoxyphenyl)amino]-4-oxobutyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 82715-98-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-4-oxo-4-[(phenylmethyl)amino]butyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



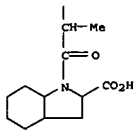
RN 82715-99-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-[[2-(3,4-dimethoxyphenyl)ethyl]amino]-1-(ethoxycarbonyl)-4-oxobutyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

PAGE 1-A

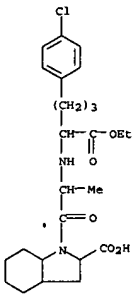


L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A



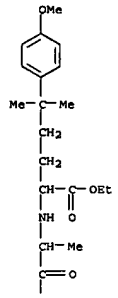
RN 82716-65-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-(4-chlorophenyl)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



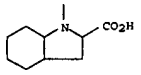
RN 82716-66-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-4-(4-methoxyphenyl)-4-methylpentyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



```
=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   213.30     380.45

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -30.75     -30.75

STN INTERNATIONAL LOGOFF AT 16:37:21 ON 12 NOV 2006
```